*Twenty-Third Annual Meeting*
*New York City, May 29-June 2, 1957*

VOLUME XXXI NUMBER 5

# DISEASES

## *of the*

# CHEST

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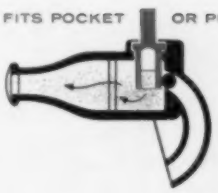


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2. Blanchard, K., and Ford R. A.: Rocky Mt. M. J. 52:278, 1955. 3. Cass, L. J., and Frederik, W. S.: Am. Pract. & Dig. Treat. 2:844, 1951.

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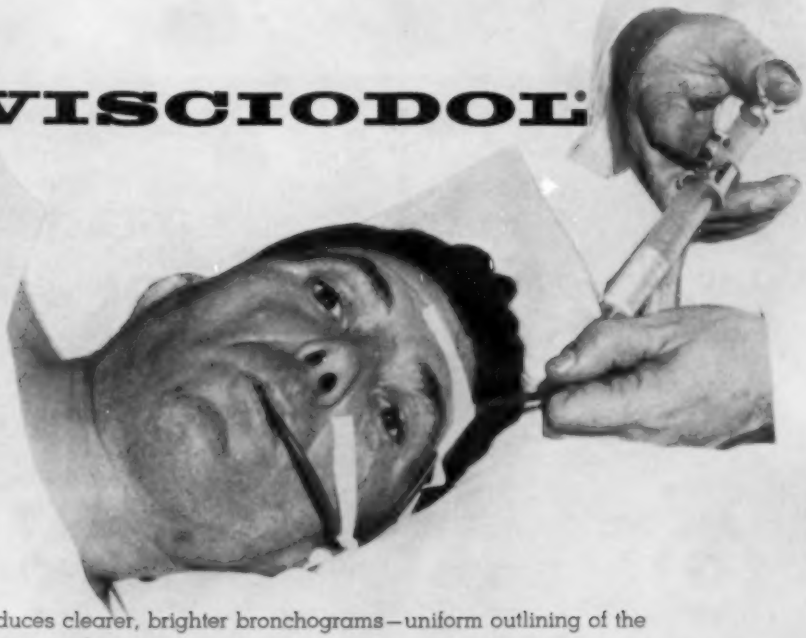

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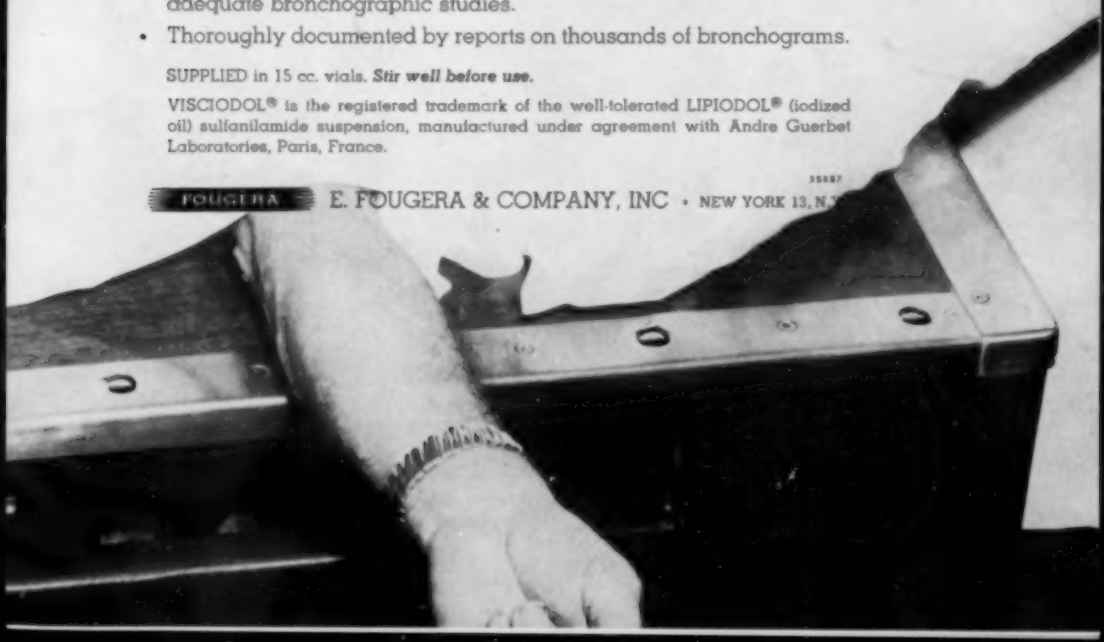

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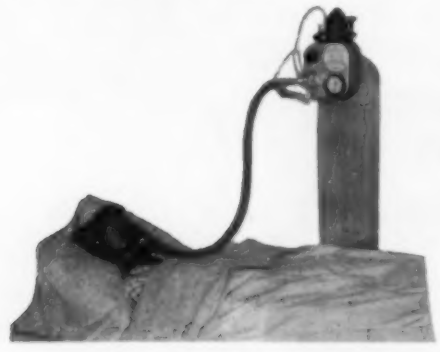

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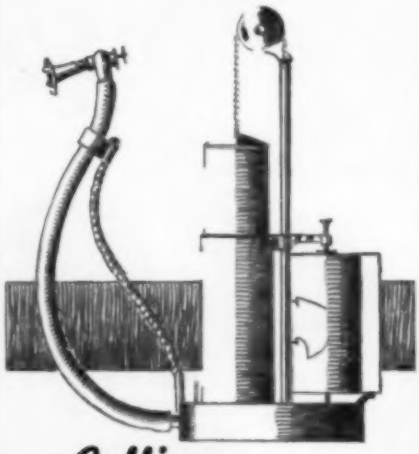

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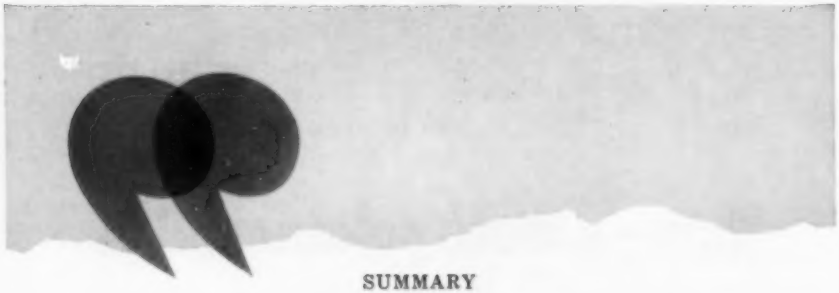


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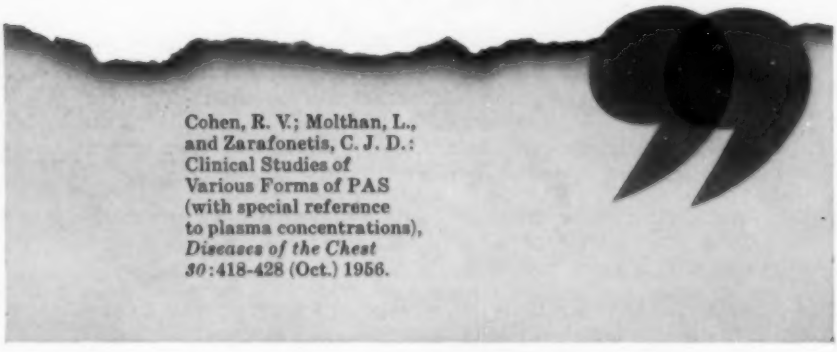


Cohen, R. V.; Molthan, L., and Zarafonetis, C. J. D.: Clinical Studies of Various Forms of PAS (with special reference to plasma concentrations), *Diseases of the Chest* *30*:418-428 (Oct.) 1956.



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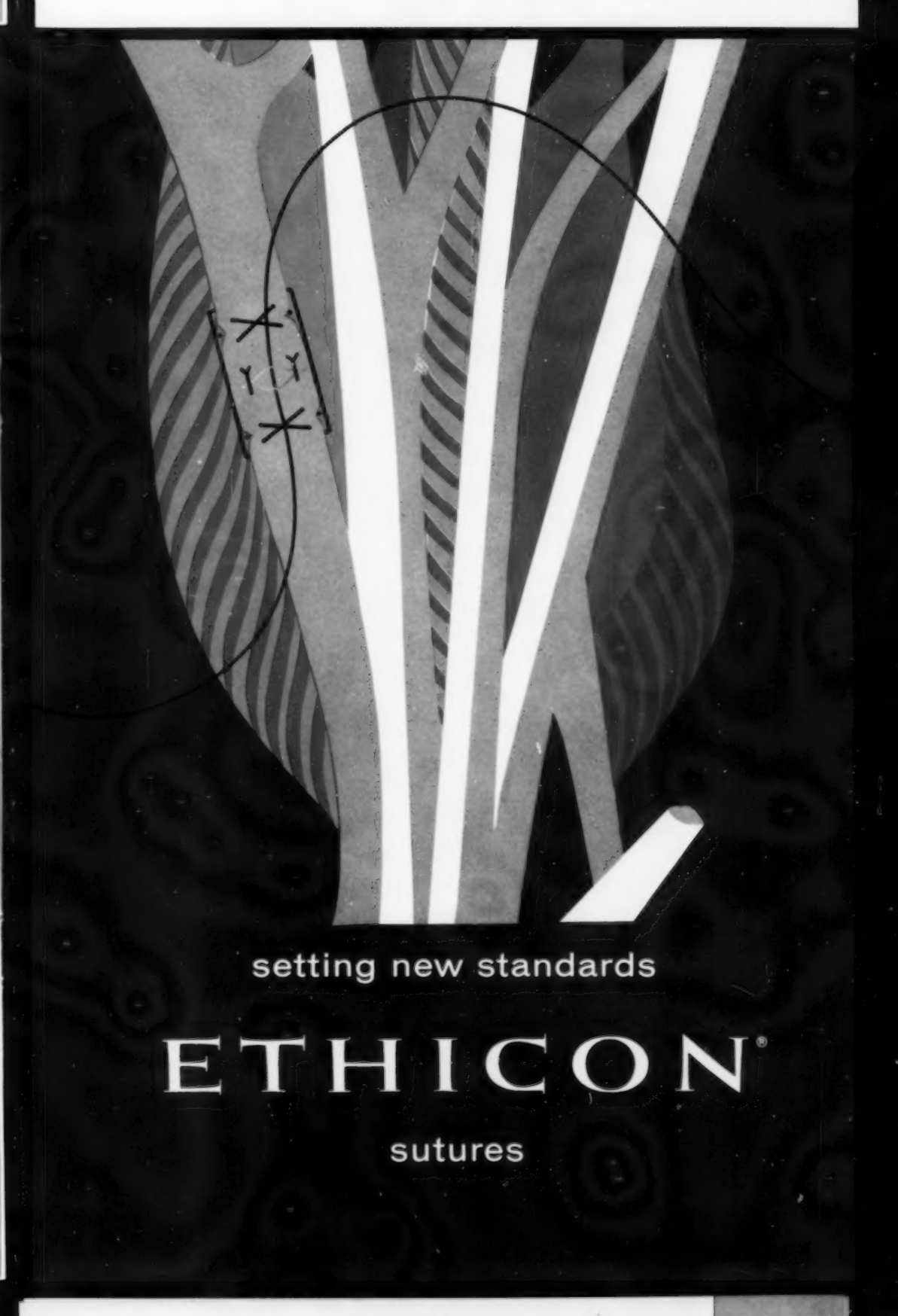
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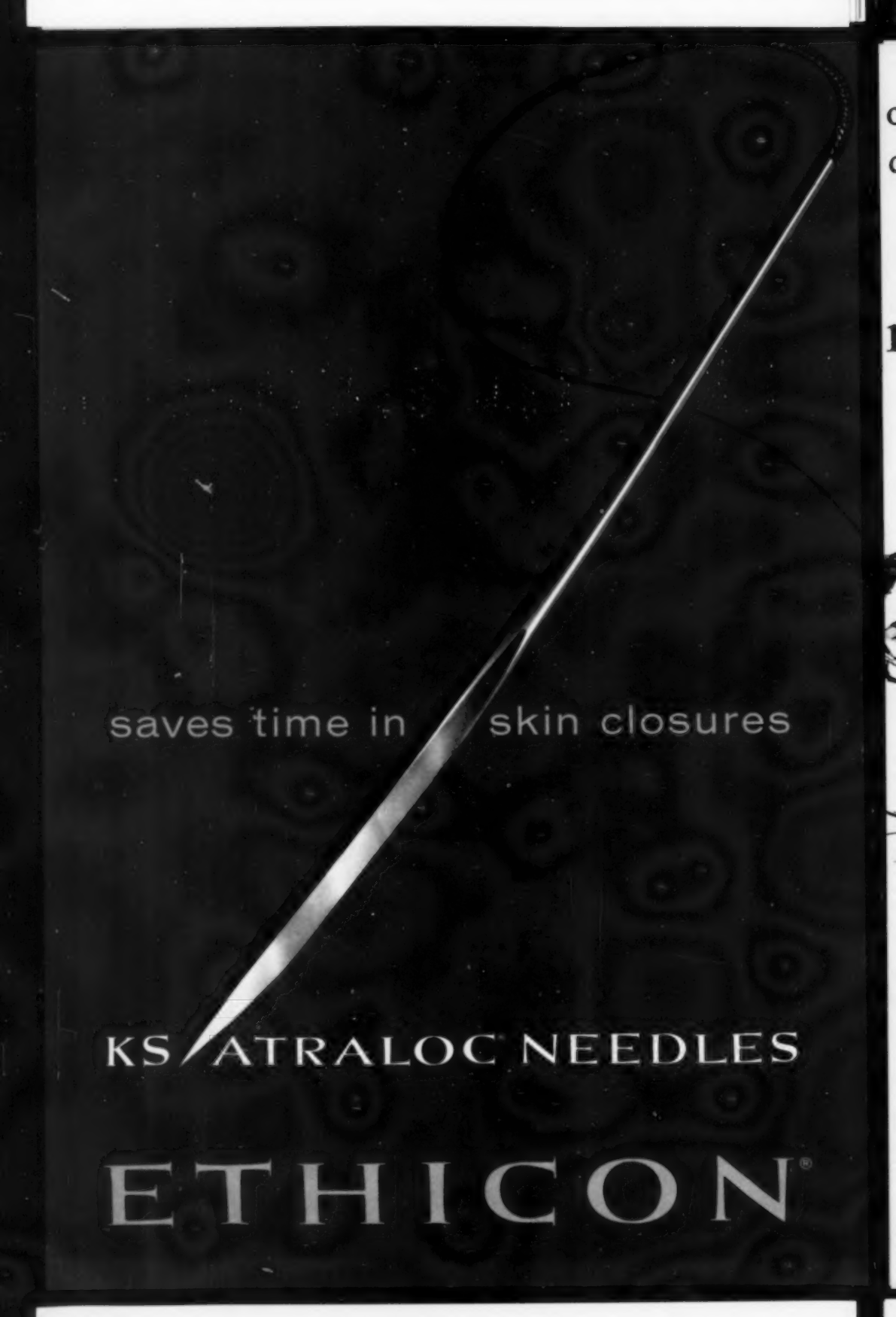
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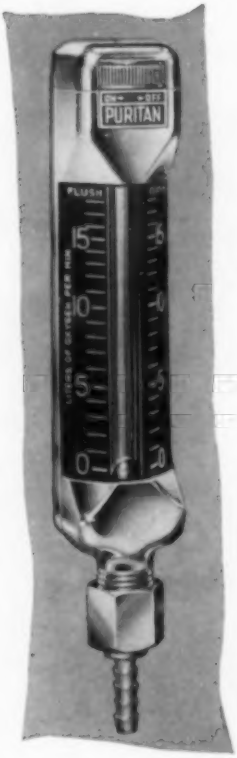


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DISEASES of the CHEST

VOLUME XXXI MAY, 1957 NUMBER 5

# The Treatment of Adenoid Cystic Carcinoma (Cylindroma) of the Respiratory Tract by Surgery and Radiation Therapy

JOHN O. VIETA, M.D. and HERBERT C. MAIER, M.D., F.C.C.P.

New York, New York

A reappraisal of the various histologic types of neoplasms arising in the trachea and major bronchi is desirable so that one can better individualize the treatment and can estimate the ultimate result with greater accuracy. A small group of endotracheal and endobronchial tumors previously often classified with the adenomas will on further study fall into the special category of cylindromas or, more accurately, adenoid cystic carcinomas of the respiratory tract.[4, 25] Although this group as a specific histologic variant has been known for many years, its growth characteristics and degree of malignancy have not been fully appreciated by some pathologists, clinicians, and thoracic surgeons.

In some classifications so-called adenomas of the bronchi are subdivided into the "carcinoid" and the "cylindroma" types. The carcinoid type is estimated to occur about 10 times as frequently as the latter. Cylindromas are found perhaps slightly more frequently in males whereas over 60 per cent of the carcinoid type occur in females.[42]

These neoplasms have been variously designated in the literature as adenoid cystic carcinoma, cylindromas, basal cell carcinomas, or mixed tumors.

Some authors, notably Womack and Graham,[49] prefer the term "mixed tumors" for adenomas, adenoid cystic carcinoma, and some other rarer neoplasms of the bronchi. Most authors[14, 22, 35] do not agree with Womack and Graham that mixed tumors of the bronchus represent a "dysembryoplasia" or disorganization of several primitive germ layers that would ordinarily form normal lung tissue. The contention that the "mixed tumors" show a similarity to mixed tumors of the salivary glands does not strengthen their viewpoint as most pathologists agree that these tumors of the salivary glands are entirely of epithelial origin. Adenoid cystic carcinoma is usually a distinct neoplasm and only occasionally noted with the "mixed tumor" form in the salivary gland.[19] Nor is the inclusion of cartilage or bone in some of the adenoid cystic carcinomas necessarily evidence for derivation from several germ layers. Such cartilage and bone may result from metaplasia, whether in the salivary glands or in the lung, or at times be remnants of bronchial cartilage invaded by tumor.

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In a more recent publication Ehrenhaft and Womack[17] have modified the conception of Graham and Womack regarding mixed tumors of the lung but still retain the terminology to depict a heterogenous group of tumors having epithelial and mesenchymal elements. In discussion of one of their cases they state "this type of tumor has been referred to by some as adenocystic basal cell carcinoma of the bronchus." It seems undesirable to include a somewhat dissimilar group of neoplasms as "mixed tumors." Furthermore many of the "malignant adenomas" reported by others[13, 23] are, as indicated by their accompanying photomicrographs, obviously examples of the neoplasm we are discussing. With the continued use of these various terms to classify histologically dissimilar entities it is impossible to accurately survey the literature to determine the frequency of occurrence, survival rate and best methods of treatment.

Belsey and Valentine[6] following the lead of Harvey's[27] study of salivary gland tumors have recommended that adenoid cystic carcinomas should be classified as a sub-group of the mucous gland tumors of the trachea and bronchi and be separated from the more usual type of adenoma of bronchus (carcinoid type) to which they are probably related. Godwin[22] in agreement with Liebow[35] and others[9, 42, 48] believes that the carcinoid type of bronchial adenoma, malignant adenoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, and mucous gland adenocarcinomas of lung are all related variants probably derived from mucous glands of the respiratory tract.

As it appears in the bronchial tree, adenoid cystic carcinoma is identical

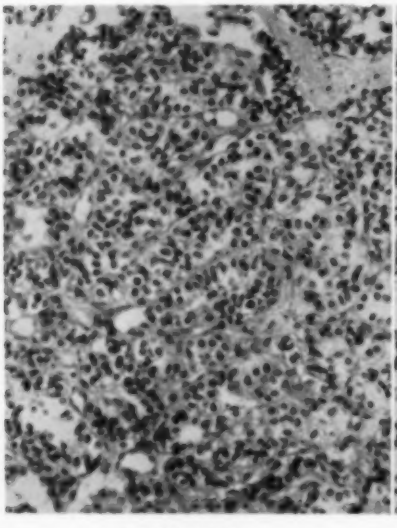

FIGURE 1

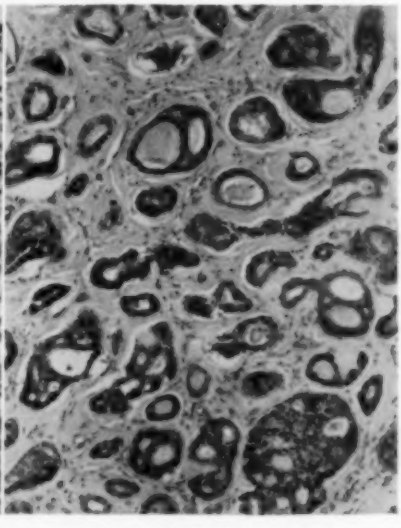

FIGURE 2

*Figure 1:* Typical carcinoid type of bronchial adenoma.—*Figure 2:* Typical adenoid cystic carcinoma showing well demarcated cell masses and spaces containing mucoid seretory material.

histologically to the tumor of the same name that occurs in the major and minor salivary glands, paranasal sinuses, lacrimal glands, mouth, nose, throat, skin, and breast. Furthermore, except for factors related to its location, its growth characteristics and clinical course are often similar to that observed when found in locations other than the respiratory tract. We, like others,[15, 20, 32] have noted that these tumors when present in anatomic sites other than the tracheo-bronchial tree, are difficult to completely eradicate locally, are occasionally radioresponsive and may recur after a long period of observation. Moreover, when metastases to the lungs are apparent the clinical course may still be prolonged for years before the demise of the patient.[3, 33] The slow progression of intrathoracic metastases was striking in two of our patients.

The histologic characteristics of the adenoid cystic carcinoma of the bronchial tree have been well described by Reid[13] and need not be reviewed here in detail. These tumors are probably derived from the bronchial mucous glands. Irregular ducts are often noted and whether the acini of the glands also take a part in the histogenesis of these growths cannot be stated with certainty. The outstanding difference between adenoid cystic carcinoma and the carcinoid of the bronchus is the presence in the former of a secretion, mucoid in type, which, with variations in the stroma, results in the characteristic histologic architecture (Figs. 1 and 2). Thus the polymorphism of these tumors is a result of interactions between the epithelial and connective tissue elements.[14, 27, 34]

Dockerty[15] has shown that the cylindromatous type of salivary gland tumor shows greater tendency to invade perineural lymphatics than other varieties. Reid's study did not emphasize perineural lymphatic invasion as a prominent feature but Belsey and Valentine specifically comment on this histologic finding in their three cases and in addition noted that in some of their histologic preparations mitoses were numerous.[6] Metastatic foci derived from adenoid cystic carcinomas may at times show such microscopic morphology that they are indistinguishable histologically from the metastases of the common types of bronchogenic cancer.[17, 23]

From the surgeon's standpoint the gross characteristics of adenoid cystic carcinomas are important. Their endoscopic appearance is variable.

TABLE I

RESULTS OF RESECTION OF MORE PERIPHERALLY LOCATED ADENOID CYSTIC CARCINOMAS OF THE BRONCHI IN WHICH LOBECTOMY OR CONVENTIONAL PNEUMONECTOMY WAS PERFORMED (9 CASES)

| | 1 mo. to 1 yr. | 1 - 2 yrs. | 2 - 3 yrs. | 3 - 4 yrs. | 4 - 5 yrs. | 5 yrs. or over | Totals |
|---|---|---|---|---|---|---|---|
| Living Without Recurrence | .... | .... | .... | (X) (X) | (X) | (X) (X) | .... |
| Living With Recurrence | .... | .... | .... | .... | .... | (X) | .... |
| Dead of Recurrent Disease | .... | .... | .... | .... | .... | (X) | .... |
| Died From Surgery | .... | .... | .... | .... | .... | .... | .... |
| No Follow-Up | .... | .... | .... | .... | .... | (X) (X) | .... |

TABLE II

COMPILATION OF RESULTS (WHERE TRACHEAL RESECTION WITH RECONSTRUCTION NOT DONE) FOR ADENOID CYSTIC CARCINOMAS LOCATED IN LARYNX, TRACHEA, MAIN BRONCHI OR PERIPHERAL BRONCHI (24 CASES)

| Author | Case No. | Location | Operation | Living | Living With Recurrence Or Residual Disease | Dead |
|---|---|---|---|---|---|---|
| Belsey 1950 | 1 | R M B | Pneumonectomy | | | 4½ months |
| MacDonald 1946 | 14 | Trachea | Laryngectomy & Tracheal Resection | 5 years | | |
| Holley 1946 | 37 | R M B | Pneumonectomy | 3 years | | |
| | 38 | L M B | Pneumonectomy | No follow-up | | |
| | 35 | L L L | Lobectomy | | 5 years | |
| Neuhof 1946 | 1 | R M B | Pneumonectomy Resection Thru Tumor at Hilum | | Several months | |
| Goldman 1950 | 4 | L M B | Pneumonectomy | 10½ years | | |
| | 9 | L M B | Pneumonectomy | | | 1 month |
| | 12 | Peripheral L L L | Lobectomy | 9½ years | | |
| | 19 | R. Mid. | Lobectomy | 9 years | | |
| | 23 | Intermed. R L L | R M & L Lobectomy | 3 years | | |
| | 25 | Peripheral L L L | Lobectomy | 3½ years | | |
| | 33 | Carina & M B | Bronchoscopy & Bronchotomy | | | 6 years. metast. |
| Doty 1951 | 4 | L M B | Pneumonectomy | 1 year well | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Moersch 1950 | 3 | L L L | Pneumonectomy | No follow-up | | |
| Enterline 1954 | 1 | R M B | Pneumonectomy | | 8 years | Died in 13 years. Last 5 years treated by x-rays and bronchoscopy |
| Ehrenhaft 1952 | 6 | L M B | Pneumonectomy & Curettage Bronchial Stump | | | less than 1 year |
| VanHazel 1949 | 12 | R M B | Pneumonectomy | | 4 years | |
| Carlens, Wiklund and Bergstrand | 1 | L M B to Carina Pericardium | Pneumonectomy & Partial Pericardiectomy Tumor at line of excision at carina | | | 6½ years. Metastases |
| | 17 | L M B | Pneumonectomy & Partial Pericardiectomy | | | 11 years. Recurrence in bronchial stump ? metastases to cervical nodes |
| | 41 | L L L | Pneumonectomy | No follow-up | | |
| | 42 | L L L | Pneumonectomy | | 4 years dyspnea | |
| | 51 | Trachea | Tracheotomy and extirpation | No follow-up | | |
| Soutter 1954 | | Intermediate Bronchus L L L | Pneumonectomy | | | Dead in 13 years of recurrence in bronchial stump and mediastinal extension |

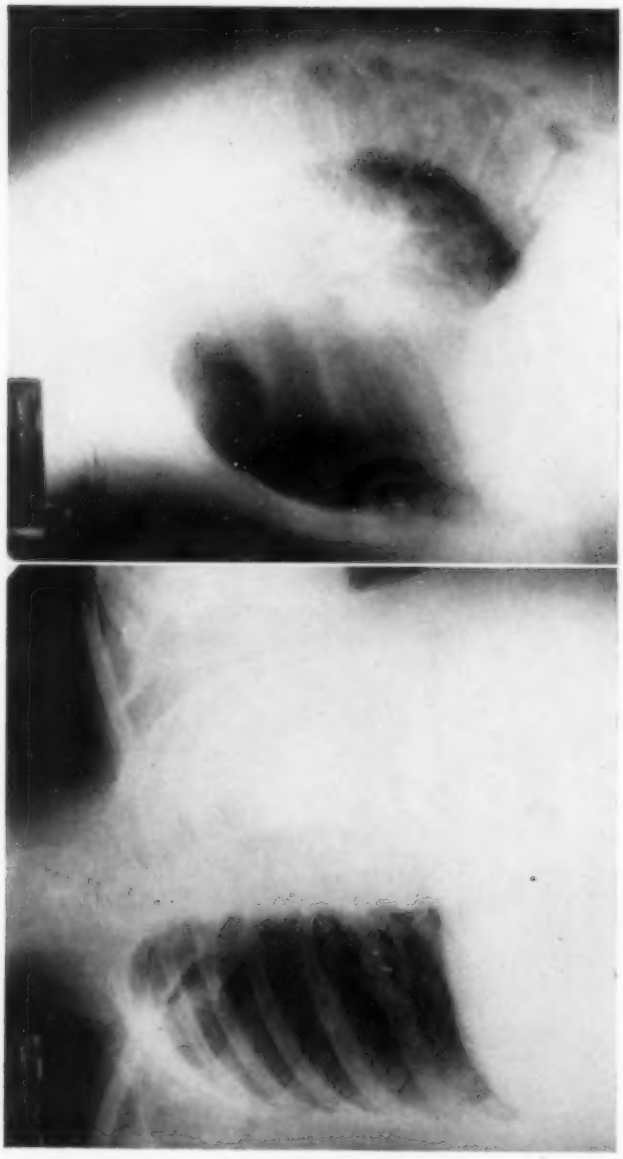

FIGURE 3 (Case 1): Radiography demonstrating displacement of trachea, mediastinum, and heart into the left chest with opacity of the left hemithorax.

They may be polypoid or broad and infiltrating. The bronchial epithelium overlying these tumors may be intact or show ulceration and squamous metaplasia. The tumors show extension submucosally so that on endoscopic or gross examination the extent of disease cannot be appreciated. Thus the base of the tumor is usually wider than its intraluminal projection. Adenoid cystic carcinomas are often found in the trachea either primarily or by extension from the primary bronchus. On the other hand carcinoid adenomas of the respiratory tract rarely involve the trachea.[18] Adenoid cystic carcinomas often extend through the wall of the trachea or bronchus so that the extraluminal infiltration into the contiguous mediastinal structures or surrounding lung tissue necessitate wide resection when surgical treatment is undertaken. As heretofore many of these tumors have been treated by endoscopic means, surgeons have not been able to gather accurate statistics on the frequency of local lymph node metastases. It must be appreciated that these tumors are of a fairly high degree of malignancy as in Enterline's[18] collected series 16 of 60 cases had metastases. Two of our patients not included in the above total developed brain metastases. From the above discussion it is apparent that the cylindroma or adenoid cystic carcinoma of the bronchial tree is to be considered a morphologic variant distinguishable histologically from other endobronchial neoplasms. Their microscopy is distinct, the clinical course may be protracted, metastases locally and to a distance are not infrequent, and their prognosis in the main is more serious than for the carcinoid type of adenoma and other types now classified by some authors as mixed tumors of the bronchus.

## *Case Reports*

*Case 1:* M. T., 48 year old white woman, was first seen by one of us (H. C. M.) in January 1943. Her history dated back to 1939 when she first noted slight dyspnea. After an extensive examination which included bronchoscopy and angiocardiography she was told that her left lung was absent. In 1941 she had her first hemoptysis. Another bronchoscopy was then done, and biopsy of the apparently blind end of the left main bronchus revealed a neoplasm instead of congenital atresia as previously diagnosed. Pathologic diagnosis was adenoid cystic carcinoma. Radiographs, as previously, showed displacement of the trachea, mediastinum, and heart into the left chest with a uniform opacity of the left hemithorax (Fig. 3). When bronchoscopy was repeated in 1943 it was found that the neoplasm had extended into the trachea for a considerable distance along the left side and had produced narrowing of the airway. Ten bronchoscopic fulgurations of the tumor in the trachea were performed in a six month period but little improvement occurred. In October 1943 exploratory thoracotomy (H. C. M.) revealed the lung to be airless and markedly shrunken. A large neoplasm occupied the central portion and extended upward into the hilum. In addition there was a large tumor mass on the anterior aspect of the hilum and another mass posteriorly intimately associated with the aortic wall but separate from the primary lesion in the lung. In view of these findings the preoperative plan of pneumonectomy with partial tracheal resection was abandoned.

Shortly after this a report of the value of radiotherapy in some cases of cylindroma came to the attention of one of us. The patient was then transferred to Memorial Hospital where radiation therapy was given. Treatment was administered on the 1000 K V apparatus with 10 cm. square portals, anterior and posterior over the trachea and mediastinum for a total dosage of 3900 r x 2 between May 25th and June 29th 1944.

Bronchoscopy in October 1944 revealed no projection of neoplasm in the trachea as previously seen. The carina was difficult to identify because of extensive stenosis of the left bronchial orifice. No tumor was seen projecting into the region of the right main bronchus as previously. There apparently had been a marked improvement due to irradiation. During 1945 she had little cough, no hemoptysis and gained weight.

On bronchoscopy in 1945 the tracheal wall appeared normal except for a slight projection into the lumen just above the carina. There was an 8 mm. orifice into the left main bronchus, visualized for 2 cm. The walls are irregular and nodular but not ulcerated. There was apparently complete occlusion of the left main bronchus 2 cm. from the carina. The mucosa seemed intact although the nodular masses were undoubtedly due to submucosal neoplasm.

Her condition remained relatively unchanged until June 1946 when there was again an increase in cough and reappearance of hemoptysis. Bronchoscopy then revealed considerable regrowth of the endobronchial lesion in the left main bronchus but the right main bronchus was not encroached upon.

Weight loss began in 1947 when metastases in the right elbow region and brain appeared. Death occurred in December 1947. No autopsy was done.

*Comment*: The clinical course was over six years from time of biopsy which established the diagnosis. The lesion had obviously been present a long time previously.

Radiotherapy showed a definite effect on the endobronchial lesion. This regression lasted for about 30 months. The clinical course demonstrates that endoscopic procedures and roentgen therapy offer palliation for the inoperable case.

*Case 2:* L. F., a 42 year old white man, was first seen at a cancer detection clinic in May 1947. A routine photoroentgen film and later conventional films disclosed numerous discrete dense nodules scattered throughout both lung fields which were interpreted as multiple metastases. A chest film that had been taken in January 1946 was reviewed and minute densities were noted in the lungs. An extensive work-up to find the primary neoplasm was undertaken but all radiographic and other laboratory tests were negative. No laryngeal examination was recorded on the chart up to this time. Later it was noted that his voice was of an unusual timbre. He offered the information that he often had voice changes during the past 15 years which were always attributed to his profession as a trial lawyer. However, laryngeal examination by Dr. Suzanne Howe showed an extensive non-ulcerated papillary mass arising from the left ventricle or false cord and involving also the posterior aspect of the epiglottis. Direct laryngoscopy confirmed the above findings and the biopsy taken was adenoid cystic carcinoma.

His general health remained excellent. He consulted one of us (H. C. M.) who advised radiotherapy to the primary lesion and, if a response was noted, roentgen therapy to the lung metastases. He decided to try a "serum therapy" for his cancer; this he received for a period of two months with no apparent benefit to the laryngeal lesion or change in the lung metastases. His only complaint was some voice change with cough at night and a sensation of a mass in his throat. A film of the chest in February 1949 showed an increase in the size of the metastatic lesions. In April 1949 he had occasional blood spitting and dyspnea. He also complained of severe frontal headaches. His hoarseness was somewhat improved but his cough interfered with sleep. Laryngeal examination revealed the mass to be slightly larger.

Under the supervision of Dr. Harriet McIntosh, radiotherapy was given to the larynx through two portals for a total of 2400 r (in air) to each port, using a 250 K V apparatus. In October 1949 he noted aphasia, memory defect and severe headaches. Examination revealed right facial weakness and cerebral involvement. Radiographs of the skull revealed no definite areas of bone lesion.

In November 1949 radiotherapy was administered to the skull with 1800 r to two portals. Following this his headache and mental confusion improved markedly but the improvement was temporary and the treatment was repeated six months later.

The laryngeal lesion showed excellent regression following radiotherapy and in April 1950 the laryngologist noted no evidence of recurrence at this site.

The lesions in the lungs were so extensive that only palliative radiation was given to the most dense collections of metastases but considerable decrease in their size resulted.

He died in December 1950. An autopsy, exclusive of the skull, showed numerous tumor nodules in both lungs. There were metastases in the right lobe of the liver; a metastasis in the left kidney, and numerous nodules on both leaves of the diaphragm. There was a 1.5 cm. nodule on the undersurface of the left ventricular fold of the larynx. The microscopic examination confirmed the biopsy diagnosis of adenoid cystic carcinoma of left ventricular fold with metastases to liver, lungs, diaphragm, and left kidney.

*Comment:* This man had demonstrable lung metastases for over four years and 9 months. The laryngeal lesion showed radiosensitivity to mod-

erate dosage and although all tumor had not been destroyed there was excellent palliation and no evidence of recurrence by clinical examination for over one year. The cerebral metastases also responded as denoted by improvement in his cerebral symptoms. The pulmonary metastases likewise showed a regression from radiotherapy.

*Clinical Features*

A localized endobronchial tumor, benign or malignant, may cause no symptom until it results in significant narrowing of the bronchial or tracheal lumen, unless hemoptysis occurs. Cough, hemoptysis and wheezing are prominent among the primary symptoms which may have been present in varying degree for weeks to years prior to definitive examination.

The symptomatology of adenoid cystic carcinoma varies with the location of the neoplasm. When the lesion is limited to the bronchus of one lung, the clinical picture is similar to that encountered in other bronchial tumors so situated. Secondary infection due to partial bronchial obstruction may obscure the preceding symptoms if such were present. If the tumor arises in the main bronchus close to the bifurcation of the trachea, signs and symptoms of tracheal obstruction may appear later. Stridor and dyspnea may be prominent features of tracheal involvement.

The roentgen findings of adenoid cystic carcinoma of the bronchus are usually similar to those encountered with other slowly growing bronchial tumors. When the tumor arises in one bronchus and extends into the lower trachea, partial obstructive emphysema of the opposite lung may develop. The routine roentgenogram is usually negative with tracheal tumors but tomography sometimes demonstrates the lesion. Bronchoscopy is the chief diagnostic procedure for adenoid cystic carcinoma because their central location usually permits visualization and biopsy.

TABLE III

RESULTS OF SURGICAL EXCISION OF ADENOID CYSTIC CARCINOMA IN LARYNX, TRACHEA, MAIN OR PERIPHERAL BRONCHI IN WHICH TRACHEAL RECONSTRUCTION WAS NOT NECESSARY OR DONE (24 CASES)

| | 1 mo. to 1 yr. | 1 - 2 yrs. | 2 - 3 yrs. | 3 - 4 yrs. | 4 - 5 yrs. | 5 yrs. or over | Totals |
|---|---|---|---|---|---|---|---|
| Living Without Recurrence | .... | (X) | .... | (X) (X) | .... | (X) (X) | |
| | .... | .... | .... | (X) | .... | (X) (X) | 8 |
| Living With Residual or Recurrent Disease | (X) | .... | .... | .... | (X) (X) | (X) | 4 |
| Dead of Recurrent or Residual Disease | (X) (X) | .... | .... | .... | .... | (X) (X) | |
| | (X) | .... | .... | .... | .... | (X) (X) | |
| | | .... | .... | .... | .... | (X) | 8 |
| No Follow-Up | | | | | | | 4 |

*Analysis of Reports in Literature*

The cases herein used for comparative purposes are not claimed to be the result of a complete review of the literature. They represent recent or readily accessible reports in which adequate data for pathologic, surgical, and radiologic considerations are available. It is only by chance that the series of cases considered for radiologic and surgical data are comparable as regards their number. There was no intention on the part of the writers to select any report in preference to others in order to support any preconceived conclusions as to the merits of one form of treatment over another.

*Surgical Considerations*

Although cylindromas have been considered to be of relatively low grade malignancy, further experience has demonstrated metastases in over 35 per cent of reported cases. Surgical resection should be given every consideration in preference to endoscopic treatment by coagulation, radon seed implantation, or use of contact radium applicators. The data in Table I indicates that when the lesion was so situated that lobectomy or pneumonectomy removed the primary growth by a wide margin the surgical results are good. Even when the tumor was more centrally located but did not require tracheal resection with reconstruction, the results are better than for most other malignant neoplasms primary in the tracheobronchial tree (Tables II and III). There is presumptive evidence that all disease could be readily extirpated in 18 of these 24 cases by conventional surgery.

This group of 18 includes one of Goldman's cases[24] with a cylindroma in the main bronchus and at the carina. This tumor was resected by bronchotomy. The patient survived six years before succumbing to metastatic disease. This illustrates that a minimal resection may in exceptional cases produce an excellent palliative result. However, a long term survival may only be a manifestation of low biological activity. For instance, one of Carlen's patients[9] with a tumor in the trachea died after five years although a tracheostomy was the only method of treatment. In five of the 24 in which resection was performed, disease was undoubtedly left behind.[9, 17, 39] Even in these five there were three long survivors. Two of them lived 6½ and 11 years respectively before death from metastases.[9] In another case[18] a recurrence in the bronchial stump was noted eight years after pneumonectomy. This patient lived five more years with the disease being controlled for the major part of that time by endoscopic coagulation and radiotherapy. This again furnishes further evidence for the prolonged course of many of these cancers.

As seen in Table III a long clinical course as exhibited by some of these neoplasms with survival of five or even 10 years does not mean that the tumor will not recur irrespective of the therapy employed. The patients reported by Belsey,[6] Carlens,[9] Enterline,[18] Goldman,[24] and Jarvis[29] illustrate this feature.

As adenoid cystic carcinomas are more often primary in the trachea

or main bronchi than in the more peripheral bronchi, a microscopic diagnosis is often available before thoracotomy. At the time of exploration and decision concerning resection this information should be given its proper evaluation. We believe that when tracheal resection of any magnitude is necessary to circumscribe gross disease it is well to remember the long clinical course exhibited in many instances by these neoplasms. Further-

TABLE IV

COMPILATION OF RESULTS WHERE TRACHEAL RESECTION AND RECONSTRUCTION WERE NECESSARY FOR EXCISION OF ADENOID CYSTIC CARCINOMA LOCATED IN TRACHEA, OR MAIN BRONCHUS EXTENDING TO CARINA

| | | | 11 Cases | | | |
|---|---|---|---|---|---|---|
| Author | Case No. | Location | Operation | Living | Living With Recurrence | Dead |
| Reid & Cahan 1952 | 1 | Trachea | Window Resection | 16 mos. | | |
| Jarvis 1950 | 1 | Trachea | Circumferential Resection | | | 33 months metastasis |
| Clagett 1952 | 1 | Trachea | Circumferential Resection & Pneumonectomy | | | 6th post-operative day |
| | 11 | Trachea | Window Resection | 11 mos. | | |
| | 4 | Trachea & R M B | Window Resection | 11 mos. | | |
| Abbott 1952 | 1 | Carina | Rt. Pneumonectomy & Reconstruction of Carina | | | 3¾ years |
| MacManus 1952 | 1 | Trachea | Circumferential Resection & End to End Anastomosis | No follow-up | | |
| Soutter 1954 | | Cervical Trachea | Partial Resection | 5 years | | |
| Belsey 1950 | 11 | R M B | Pneumonectomy | | Recurred in 6 yrs. in Trachea Then Tracheal Window Resection. Residual Disease Left at Time of Surgery 18 mos. | |
| | 3 | Trachea | Window Resection Then Again Window Resection | | Recurred in 1 year | 15 months after last resection Autopsy: Recurrence in Rt. Main Bronchus & Trachea |
| Carlens 1954 | 24 | Trachea | Tracheal Resection | 1 year | | |

more radiotherapy and endoscopic treatment may often palliate the presenting symptoms and extend life without the attendant risk of pneumonnectomy plus trachial reconstruction. There are others, however, who are of the opinion that restoration of an adequate airway by pulmonary resection and tracheoplasty may justify palliative excisional surgery.[6] Although the results of tracheal excisions, with or without concomitant pulmonary resection, seem to indicate favorable short term successes[1, 5, 8, 10, 11, 29, 36, 45] we agree with Belsey who anticipates that the late results of tracheal resection will be disappointing in regard to long term survival. For local removal the problem ideally resolves itself into a resection with a wide margin of normal tracheal or bronchial wall with or without sacrifice of distal pulmonary tissue. Anatomic considerations may make this desideratum impossible to carry out.

Due to the growth characteristics of this neoplasm it is apparent that the lines of excision should be checked by frozen section tissue analysis in order that the limits of the submucosal and extramural spread of disease may be determined and adequate excision performed. We raise the question also whether it would not be advisable to do mediastinal lymph node dissection as well in view of the propensity for metastases locally. In the patients who have had conventional pneumonectomy with or without tracheal resection and reconstruction, it is noted that recurrence in the trachea and bronchi is more frequent than one should expect with radical excisional surgery. Patients reported by Belsey, Carlens, Ehrenhaft, Enterline, Soutter, and Goldman, are cases in point.

The various methods of repair of surgically created tracheal defects have been reviewed by Cotton.[12] Since Belsey's original publication re-

TABLE V

RESULTS OF RADIOTHERAPY FOR ADENOID CYSTIC CARCINOMA OF THE TRACHEO-BRONCHIAL TREE COLLECTED SERIES—31 CASES

| | 1 mo. to 1 yr. | 1 - 2 yrs. | 2 - 3 yrs. | 3 - 4 yrs. | 4 - 5 yrs. | 5 yrs. or over | Totals |
|---|---|---|---|---|---|---|---|
| Living Without Recurrence | X | .... | (X) | (X) X | .... | (X) (X) | |
| | | .... | .... | .... | .... | (X) (X) | |
| | | .... | .... | .... | .... | X X | 10 |
| Living With Recurrent or Residual Disease | | (X) | X | .... | .... | X | 3 |
| Dead of Disease | X | .... | (X) | .... | X | (X) (X) | |
| | (X) (X) | .... | X | .... | .... | X X X | 11 |
| No Follow-up | (X) (X) (X) (X) (X) (X) (X) | | | | | | 7 |

(X) Cases Collected Prior to 1945. X Cases Reported after 1945.

garding the intrathoracic resection of the human trachea, several reconstructive techniques have been used but should be considered still in the developmental stage. Only further experience will determine which of the methods of tracheoplasty[8, 21, 40] will be the most successful and carry the least morbidity. From published reports the immediate mortality rate for resection of the intrathoracic trachea for cylindroma is low but one wonders if this is because of selective reporting.

A perusal of the surgical results of extirpation of adenoid cystic carcinomas of the respiratory tract as noted in Tables I, II, III, and IV reveals that no one to date has had sufficiently extensive experience in resection of tracheobronchial tumors of this type to warrant any conclusion as to the best modality of treatment. There is a definite trend toward more radical surgical extirpation. Experience with cylindromas in more accessible areas would tend to indicate that few cylindromas of the trachea will be permanently cured by the limited surgical excisions that have been done in the past or are now possible. Frazell[20] in analyzing results of therapy for adenoid cystic carcinomas of the major salivary glands, readily accessible areas, reports a 24 per cent five year survival rate.

The results or resection of those lesions necessitating some type of tracheal resection and reconstruction are noted in Table IV. One cannot draw conclusions regarding this material as the follow-up is too short. Of the 11 cases there is one five year survival for a resection of the cervical trachea; three have died of recurrent disease; one is living with residual cancer at 18 months; one died post-operatively; in one there is no follow-up but presumed to be living; and in four the follow-up is less than 3½ years. From this data it is apparent that late results cannot be viewed optimistically.

TABLE VI

RESULTS OF SURGICAL EXCISION OF ADENOID CYSTIC CARCINOMA ALL CASES REGARDLESS OF LOCATION IN TRACHEO-BRONCHIAL TREE—(35 CASES)—COLLECTED SERIES

| | 1 mo. to 1 yr. | 1 - 2 yrs. | 2 - 3 yrs. | 3 - 4 yrs. | 4 - 5 yrs. | 5 yrs. or over | Totals |
|---|---|---|---|---|---|---|---|
| Living Without Recurrence | (X) (X) (X) | (X) X | .... | X X X | .... | X X X X (X) | 13 |
| Living With Residual or Recurrent Disease | X | (X) | .... | .... | X X | X | 5 |
| Dead of Recurrent Or Residual Disease | X X X | (X) (X) | .... | (X) | .... | X X X X X | 11 |
| Died From Surgery | (X) in 6 days | .... | .... | .... | .... | .... | 1 |
| No Follow-up | X X (X)<br>X X | ....<br>.... | ....<br>.... | ....<br>.... | ....<br>.... | .... | 5 |

(X) Resections with Tracheal Reconstruction. X Resections Wherein Tracheal Reconstructions Not Necessary or Not Done.

*Radiotherapeutic Considerations*

There is a difference of opinion in the literature regarding the response of the adenoid cystic carcinomas to radiotherapy. Some observers state that these neoplasms are radiosensitive; others that the tumors are radioresistant. A more accurate appraisal would seem to indicate that these tumors sometimes do respond to radiation therapy to a striking degree while in other cases the therapeutic results have been disappointing. Most authors agree that the carcinoid adenoma does not usually respond to radiation. In not having differentiated the adenoid cystic carcinomas as distinct in behavior from the carcinoid group many have concluded that the cylindroma would respond to radiotherapy in a similar manner. When adequate surgical resection cannot be carried out, recourse to radiotherapy may result in growth restraint. If in addition bronchoscopic resection and coagulation is able to remove some of the growth so that there is amelioration of tracheal and bronchial obstruction, some of these patients may live in relative comfort for some years.

Baclesse[3] states that for the best results in any radioresistant tumor the therapy should be given over a long period of time and through small portals. He and Lampe,[3, 33] reporting on adenoid cystic carcinomas of the salivary glands and mouth, noted the tumors to be radioresponsive and palliated by this therapy.

Kramer and Som[30] have reported some patients with cylindromas who showed marked benefit from radiotherapy and they demonstrated that irradiation is a valuable adjuvant to the treatment of this cancer in the upper respiratory tract.

The authors have collected 31 cases of cylindroma of the tracheobronchial tree that were treated by radiotherapy alone or used in conjunction with bronchoscopic procedures. The majority of the patients treated by radiotherapy and endoscopic procedures were those who had a lesion in the larynx, trachea, or main bronchus extending into the trachea. Nineteen of the 31 patients were treated by radiotherapy prior to 1945, and 12 since that date. It is only in the past 10 years that modern techniques for tracheo-bronchial resection and reconstruction have been evolved. Prior to Belsey's report it is apparent that radiotherapy and/or endoscopic procedures were the only therapeutic measures available for that group of patients with cylindromas arising or extending into the lower trachea. With the advent of techniques for tracheal reconstruction, it is noted that the trend of therapy is toward surgical resection and away from radiotherapy. Understandably some patients who have had exploratory surgery but in whom resection could not be performed will gravitate to the radiologist for last resort therapy. It would seem apparent that the non-resectable and recurrent cases would be the patients with the poorest ultimate prognosis as they would undoubtedly represent the group with the most extensive disease.

From a review of the methods used to treat these 31 patients where radiation therapy was considered to be an important part of the manage-

ment, it is to be emphasized that there was no uniformity in the radiotherapeutic modalities. Some were treated with contact radium applicators, others by radon seed implantation, and others by external therapy with standard voltage equipment. There is an inadequate experience to date with the use of supervoltage roentgen therapy. We believe this type of equipment would be that of choice for the treatment of those lesions in the lower trachea when surgery is not elected or cannot be performed. Objective evidence to support this viewpoint was noted in our Case 1. Even in this patient the maximum radiotherapeutic effort was not carried out according to present standards of treatment. Rotation therapy would be a modification that should be explored for its potentialities in treating adenoid cystic carcinoma in the trachea and adjacent tissues.

In order to tabulate a comparable series of patients treated by radiologic methods cases reported prior to 1945 are grouped with those reported since that date. The radiologic group can then be compared with the surgical group.

Analysis of Table V yields the following observations. Of 31 cases treated by radiotherapy, (sometimes supplemented by endoscopic procedures) six were living without recurrence over five years; five died of disease in five or more years; one was living with recurrent disease after five years; four others were living from several months to four years without recurrence; two were living with recurrent or residual disease from one to three years; six had died of disease in from a few months to four years; in seven there was inadequate data to determine the effects of therapy.

Marked palliative benefits for inoperable cases can be expected in over one third of the patients with cylindromas of the tracheobronchial tree if judicious roentgen therapy is used. The degree of palliation for inoperable or recurrent cases is well documented in those patients reported by Reid, Enterline, Goldman, and ourselves. The above data appear to indicate that

TABLE VII

COMPARISON OF RESULTS OF METHODS OF TREATMENT FOR ADENOID CYSTIC CARCINOMA OF THE TRACHEO-BRONCHIAL TREE

| | Living Without Recurrence 1 mo.-5 yrs. | Living With Recurrent or Residual Dis. 1 mo. to 5 yrs. or over | Alive Without Evidence of Recurrence 5 yrs. or over | Dead of Disease 1 mo. to 10 yrs. After Treatment | No Follow Up | Totals |
|---|---|---|---|---|---|---|
| Patients Treated by Radiotherapy With or Without Additive Endoscopy | 4 | 3 | 6 | 11 | 7 | 31 |
| Patients Treated by Surgery | 8 | 5 | 5 | 11 | 5 | 35* |

*(Including one post-operative death)

roentgen therapy should still occupy a prominent position in the management of some of these neoplasms.

### *Comparison of the Results Obtained by Radiation Therapy (With or Without Additive Endoscopy) and Surgical Resection*

Only a few remarks are necessary to show the comparison in modalities of treatment. The reader may draw his own conclusions from the tabulated data. If only the five year end result is used as a yardstick of successful therapy it is noted that of 31 cases treated by radiologic methods six lived five or more years without recurrent disease and one other was living with recurrent or residual disease five or more years. It is also noted that of 11 already dead five lived for five years before demise.

Among the 35 patients treated by various types of excisional surgery (Table VI), five were living without demonstrable disease five or more years; and one was living with recurrent or residual disease for over five years. There are 12 patients, including one who died in the postoperative period, who are already dead in periods of from several months to over five years. It is probable that in those without a long term follow-up similar percentages of successes and failures will appear with the passage of time.

In Table VII the above data regarding results of surgical and radiologic therapy are summarized. Failure to effect a cure by either modality of therapy is not synonymous with failure of treatment since a fair percentage of the patients were well or helped symptomatically for long periods of time.

### *Discussion*

Adenoid cystic carcinomas or cylindromas of the tracheobronchial tree are histologically similar to certain neoplasms occurring in the major or minor salivary glands, nasal sinuses, pharynx, palate and other locations. These tumors are apparently derived from mucous glands or ducts occurring in these anatomic areas. In the tracheobronchial tree they are likewise infiltrating tumors with a rather prolonged course in many instances. However, this neoplasm ultimately shows a rather high incidence of metastases both locally to lymph nodes and to distant areas. Their clinical course and much poorer prognosis should distinguish the cylindromas from the carcinoid type of bronchial adenoma which has a comparatively benign clinical course and from other "mixed tumor" types of the tracheobronchial tree with which they are often grouped.

The results of either surgical or radiologic treatment of cylindromas combined with endoscopic procedures cannot be considered good although the results are better than for the common cancers of the tracheobronchial tree. Apparently when the neoplasm is so situated anatomically that lobectomy or pneumonectomy is possible the therapeutic results are relatively good. However, when the neoplasm extends into the mediastinum or when tracheal resection of any extent is necessary to circumscribe gross disease, a critical re-evaluation at the time of surgery should be made; the operative mortality weighed, and radiation therapy should be seriously consid-

ered. It is apparent that five year survival without demonstrable disease does not necessarily mean cure by surgery or radio-therapy. This tumor is slow growing in so many instances that the history of the disease must be appreciated before any claim as to superiority of one form of therapy over another is made. The role of tracheal resection has still to be evaluated. Data on the results of supervoltage radiotherapy for this neoplasm are lacking. Symptomatic relief that follows restoration of an airway may justify palliative resection but the same may be accomplished often by endoscopic measures and radiotherapy.

## SUMMARY

The pathologic and clinical features of adenoid cystic carcinomas or cylindromas of the tracheobronchial tree have been reviewed and compared with certain other bronchial neoplasms. This is a neoplasm of moderately high malignancy with pronounced infiltrative qualities and exhibits metastases in over a third of reported cases. Although the prognosis is often doubtful as to cure, life expectancy may be reckoned in terms of years.

Therapeutic results obtained by surgery and radiotherapy have been evaluated. At the present time one would advocate surgical exploration and resection of these tumors if they are of limited extent. If the tumor cannot be safely removed one may consider abandoning resection and plan palliative therapy by radiologic methods. This applies particularly to tracheal lesions near the carina. The reasons for this viewpoint have been discussed.

Two cases are reported which showed distant metastases. Roentgen therapy directed to the primary and metastatic lesions was of marked palliative benefit to these patients for prolonged periods of time.

## RESUMEN

Las características clínicas y patológicas del carcinoma quístico adenoide o cilindroma del árboi traqueobronquial se han revisado y se comparan con algunos otros neoplasmas. Este es un neoplasma de moderada malignidad con características infiltrantes marcadas y que presenta metástasis en más de un tercio de los casos relatados. Aunque el pronóstico es a menudo dudoso en lo referente a curación, las probabilidad es de tiempo de sobrevida son de calcularse en años.

Los resultados terapéuticos obtenidos por la cirugía y por la radioterapia se han estimado. Actualmente es de aconsejarse la exploración quirúrgica y resección de estos tumores si son de extensión limitada. Si el tumor no puede extirparse con seguridad puede considerarse el abandonar la operatión y hacer paliación radiológica. Esto es aplicable especialmente a las lesiones traqueales cerca de la carina. Se discuten las razones para este punto de vista.

Se relatan dos casos que mostraron metástasis a distancia. La roentgenterapia dirigida a las lesiones primarias y metastásicas produjo marcado efecto paliativo en estos enfermos por largo tiempo.

ZUSAMMENFASSUNG

Es werden die pathologisch-anatomischen und die klinischen Merkmale der adenoiden cystischen Carcinome oder Cylindrome des Tracheo-Bronchialbaumes einer Durchsicht unterzogen und mit bestimmten anderen bronchialen Neoplasmen verglichen. Es handelt sich um ein Neoplasma mässigen Grades von Bösartigkeit mit ausgesprochen infiltrativen Eigenschaften, das in mehr als einem Drittel der mitgeteilten Fällen Metastasen aufweist. Obgleich die Prognose hinsichtlich einer Heilung oft zweifelhaft ist, kann man doch mit einer Lebenserwartung von Jahren rechnen.

Die therapeutischen Ergebnisse, wie sie die Chirurgie und die Strahlentherapie zustandebringen, erfahren eine Auswertung. Zum gegenwärtigen Zeitpunkt wird man chirurgische Untersuchung und Resektion dieser Tumoren empfehlen, sofern sie von begrenzter Ausdehnung sind. Kann jedoch der Tumor nicht mit Sicherheit entfernt werden, so wird man in Erwägung ziehen, die Resektion aufzugeben und palliative Therapie mit radiologischen Methoden in die Planung einzubeziehen. Dies gilt besonders von trachealen Herden nahe der Bifurkation. Die Gründe für diesen Standpunkt werden besprochen.

Zwei Fälle werden vorgestellt, die entfernt gelegene Metastasen zeigten. Die gegen die primären und die metastatischen Herde gerichtete Röntgentherapie war von ausgesprochenem palliativen Vorteil für diese Patienten über längere Zeitabschnitte.

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# The Value of Serum Aminopherase Determinations in Suspected Acute Myocardial Infarction*

SEYMOURE KRAUSE, M.D., F.C.C.P.,** EDWARD W. HECKERT, M.D.,†
PASQUALE SOLINAS, M.D.†† and IRWIN M. BOGARAD, M.D.§
Pittsburgh, Pennsylvania

At the present time when a physician is confronted with a patient who has persistent chest pain or epigastric distress that is thought to be cardiac in origin, the electrocardiogram is usually considered to be the final criterion in determining whether acute myocardial infarction has occurred. Frequently, however, the electrocardiogram taken soon after an acute myocardial infarction occurs may fail to confirm the correct clinical impression, and the patient is denied early adequate therapy. In addition, the unsuspecting physician who is lulled into a false sense of security by an electrocardiogram that is not diagnostic of recent infarction, may neglect to obtain serial electrocardiographic studies, or he looks elsewhere for a diagnosis that will explain the patient's symptoms.

A chemical test to aid in the detection of myocardial injury would seem highly desirable. In 1941 Cohen and Hekhuis reported that certain animal tissues were rich in glutamic oxaloacetic aminopherase (transaminase) and that the concentration of this enzyme was particularly high in the myocardium.[1] Based on these facts, LaDue and his associates investigated the serum level of this enzyme in healthy individuals, those with diverse types of cardiac dysfunction and patients with a large variety of other illnesses.[2, 3] Their data, and subsequently that of other investigators, indicated that there was a 2-20 fold increase in the normal serum transaminase immediately following myocardial injury.[4, 5, 6]

The chemical determination of serum transaminase is based on the oxidation of reduced diphosphopyridine in the presence of malic dehydrogenase. This reaction proceeds when transamination occurs in the primary reaction involving the transfer of the alpha-amino nitrogen of aspartic acid to alpha-ketoglutaric acid to form glutamate and oxaloacetate. The actual assay is spectrophotometric one which detects the decrease in optical density as this reaction proceeds. One unit has been defined as the equivalent of the change in optical density of .001 per cc. of serum per minute at a wave length of 340 mu. All reagents are used in excess and the limiting factor to the reaction is the quantity of serum transaminase activity in the serum. The serum enzyme is stable at freezing temperature for about two weeks. The normal range of serum transaminase is from 10-40 units.[7]

*From the Montefiore Hospital Institute of Research, Pittsburgh, Pennsylvania and the Veterans Administration Hospital, Pittsburgh, Pennsylvania.
**Research Associate.
†VA Hospital.
††Resident in Medicine (presently in Perugia, Italy).
§Resident in Medicine.

Our records include cases of clinically and electrocardiographically proved recent myocardial infarction, and a variety of both medical and surgical diseases. Early experience with the assay indicated that the serum enzyme level rose sharply within 24 hours after the acute infarct; consequently it is our practice to obtain samples when the diagnosis is first suspected and then daily for at least three successive days. The serum transaminase concentration can fall quite rapidly and approaches the normal range within a week of the original episode. There are certain disease entities in addition to acute myocardial infarction; however, that will give elevated serum transaminase values. Liver, skeletal muscle, and kidney are normally rich in transaminase and severe active involvement of these tissues will result in an elevation of the serum transaminase value above the normal range.[8] There is evidence to suggest, however, that the curves obtained with these acute processes are different from those seen in acute myocardial infarction. Furthermore, the situations that can result in elevated serum transaminase levels are usually differentiated clinically from a recent myocardial infarction.

Our data correlates well with that of LaDue, Kattus and other investigators. It is our purpose in this report to cite some of the clinical situations where the determination of the serum transaminase has been of particular value indicating the presence or absence of acute myocardial infarction. In simple terms, this can best be stated as those instances where the electrocardiogram is not diagnostic of acute myocardial infarction. Recognizing that the electrocardiogram has limitations, it is still considered the laboratory procedure that best confirms or denies the presence of acute myocardial injury with or without associated tissue necrosis. The following case reports emphasize electrocardiographic limitations, and hence the value of serial serum transaminase determinations in the diagnosis of acute myocardial injury.

1. The serum transaminase may be elevated before a diagnostic electrocardiogram appears.

Every clinician has had the experience of being confronted with a patient who has a history compatible with myocardial infarction, but on whom the electrocardiogram denied confirmation of this clinical diagnosis within the first few days of hospitalization. In these cases we have used the elevation of serum transaminase to reinforce our clinical judgment, so that we could start adequate therapy early. Furthermore, it has helped us speak with assurance to the patient and his family about the diagnosis at an earlier date than if one awaited the results of several electrocardiograms for confirmation.

*Case 1:* S. H., a 53 year old, colored man was admitted on February 25, 1956 with a five day history of epigastric discomfort and a burning sensation radiating to the precordium. This latter pain was relieved by rest. For the past two months he had had a productive cough, dyspnea, and five pound loss of weight. There was no previous cardio-respiratory symptom. He had a right inguinal herniorrhaphy in 1954. Physical examination revealed a well developed and well nourished individual in no acute distress. The thorax was hyperresonant, with limited expansion on deep inspiration. The heart rate was regular at 80/minute with the sounds distant. The blood pressure was 140/86 mm. Hg. The liver, spleen, and kidneys were not palpable, and there was no abdominal

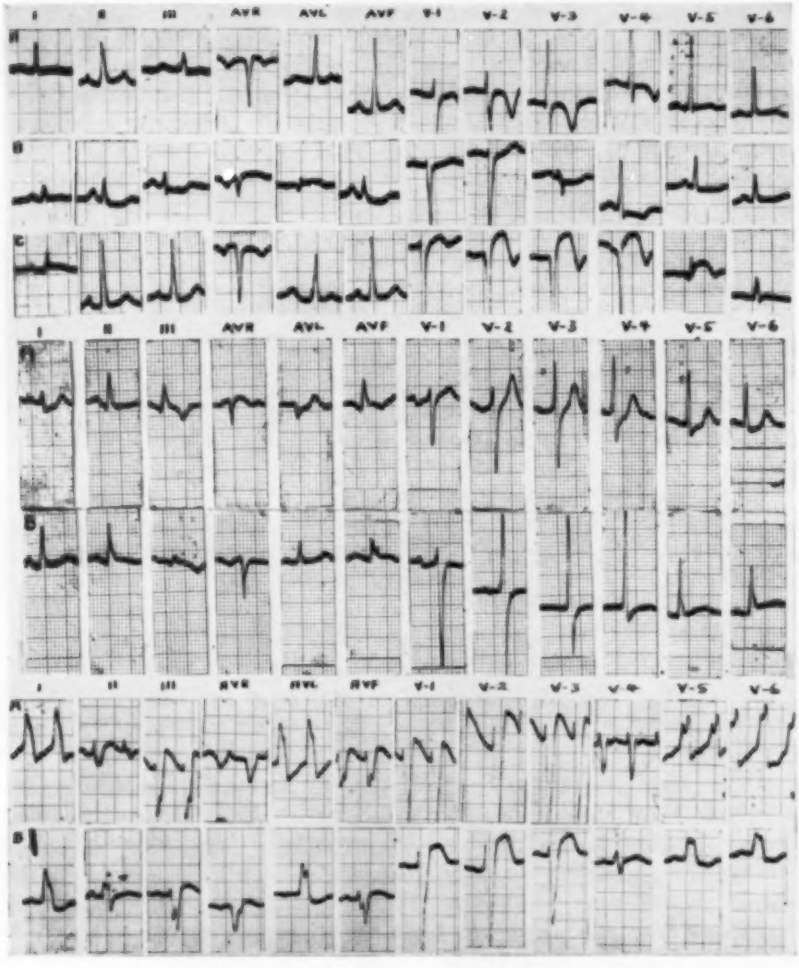


FIG. 1




FIG. 2




FIG. 3

*Figure 1:* Tracing A—T wave flat in lead one; inverted in V2, V3, and V4. Tracing B-ST now depressed in lead 2, lead 3, AVF, V4, V5. Tracing C-ST elevated in lead 1, V2, V3, V4, V5. Coving of the ST segment in V2, V3, V4, and V5. R wave now absent in V2, V3 and V4; small Q wave in V5. The serum transaminase was 440 units on February 28, several days before there was definite evidence of acute myocardial infarction. *Figure 2:* Tracing A—ST depressed in lead one, V4, V5, and V6. Small Q wave in lead 2, lead 3, AVF. Flat T wave in lead 2; inverted T wave in lead 3 and AVF. Tracing B—ST deviations no longer apparent. T wave flattened in V2, V3, V4, V5, and V6. The normal serum transaminase values are more consistent with recent pulmonary infarction than acute myocardial infarction. *Figure 3:* Tracing A—shows ventricular tachycardia; no definite evidence of recent myocardial infarction. Tracing B—Elevation of the ST segments in leads V1, V2, V3 with coving. The elevated transaminase value at the time of Tracing A was consistent with a recent myocardial infarction that was later confirmed by the electrocardiogram.

tenderness. The extremities were free of edema. The tendon reflexes were equal and active. On February 27, 1956 he first experienced severe substernal pain with an increase in dyspnea and nausea. Examination revealed a bigeminal rhythm, and he was placed on quinidine. Serial electrocardiograms were interpreted as "myocardial anoxia" until March 2 when there was definite evidence of recent anterior myocardial infarction (Figure 1). From February 28 to March 3 he had several episodes of precordial pain which were relieved by narcotics. The transaminase was 440 on February 28 and 260 on February 29. Urinalysis and blood count were normal. The sedimentation rate on March 2 was 21 mm. per hour. The blood sugar, N. P. N., total protein and serum cholesterol was normal, and the serology was negative. A chest x-ray film revealed slight, generalized cardiac enlargement and calcification of aorta. Treatment consisted of narcotics, heparin, dicumarol, quinidine, tincture of belladonna, antacids, and oxygen. He was discharged on March 29, 1956 in good condition.

2. The serum transaminase may aid in the differential diagnosis between pulmonary and myocardial infarction.

Another instance where the serum transaminase can be of value is in the differential diagnosis between pulmonary and myocardial infarction. The electrocardiographic representation of both entities has been frequently described, but unfortunately clear cut diagnostic criteria are not always present.[9] Recent experimental and clinical data have confirmed the impression that the presence of an acute pulmonary infarction will not result in an elevated serum transaminase level, such as occurs with acute myocardial infarction.[10] This is because of the abundance of serum transaminase in heart muscle and the relatively small amounts in pulmonary tissue.[11] The following case of pulmonary embolism with pulmonary infarction demonstrates the value of transaminase determination when acute myocardial infarction is suspected clinically.

*Case 2:* A. S., a 51 year old white man was admitted on May 25, 1955 with the history of being awakened that day with severe pain in the left side of his chest which was followed by profuse sweating. He complained of palpitation and was coughing on admission. He reported having had an acute myocardial infarction three years previously. Physical examination revealed an apprehensive white man in acute distress. The skin of the extremities and the nailbeds was cyanotic. There were rales at the left lung base. Blood pressure was 110/70. The heart rate was regular at 130/minute, and there was a Grade I systolic murmur at the apex. The heart was considerably enlarged to the left. The liver, spleen and kidneys were not palpable. There was no peripheral edema. On May 27 urinalysis, blood sugar, N. P. N., and hemoglobin were normal. The white blood cell count was 10,900/cu.mm. with 75 per cent polymorphonuclear leukocytes. Sedimentation rate was 25 mm/hour. The chest x-ray film demonstrated generalized cardiac enlargement with bilateral hilar thickening. After the first hospital day he was asymptomatic and afebrile. His chest became clear to auscultation. The blood pressure was 124/80 with a pulse rate of 85. The transaminase values were 18 units on May 28, 26 units on May 29 and 14 units on May 30. He was treated with oxygen, narcotics, sedation, digitalis, diamox, heparin, dicumarol and atropine, and was discharged on June 5 in good condition. The electrocardiogram of May 28 shows the evidence of the old posterior wall myocardial infarction and probably the changes of his recent pulmonary infarction (Figure 2).

3. An elevated serum transaminase may confirm an acute myocardial infarction in the presence of a cardiac arrhythmia.

Frequently, arrhythmias are associated with recent myocardial infarct. When the cardiac rate is rapid there may be difficulty in defining ST deviations. Paroxysmal arrhythmias also have certain electrocardiographic features that resemble the changes produced by myocardial anoxia, and these may be so interpreted in the absence of a recent infarct. The electrocardiographic contour of ventricular arrhythmias in particular may resemble a recent myocardial infarct in certain of its features. The following

case demonstrates the value of an elevated transaminase level in confirming the clinical impression of an acute myocardial infarction when the electrocardiogram displays a ventricular tachycardia.

*Case 3:* S. E., a 55 year old white woman was admitted on December 2, 1955 with a history of being awakened with constant substernal pain and numbness in the right arm. She experienced dyspnea and orthopnea with much belching and intermittent palpitations. She had been on a daily maintenance dose of digitalis and frequent diuretics for the treatment of congestive failure. She gave history of a myocardial infarct in 1953. Physical examination revealed an acutely ill and dyspneic patient. There was no evidence of increased venous pressure. The lungs contained bilateral moist rales at the bases. The blood pressure was 110/70. The heart rhythm was slightly irregular at a rate of 180/minute. Abdominal examination revealed no organomegaly. The lower extremities had a Grade I pitting edema. The urine contained a trace of albumin and 1-3 white blood cell count per high power field with occasional hyaline casts. The hematogram was normal except for 88 per cent polymorphonuclear leukocytes. The sedimentation rate, blood sugar and N. P. N. were normal, and the blood serology was negative. The electrocardiogram of December 2, 1955 (Figure 3) exhibited a ventricular tachycardia, which was subsequently converted to a normal sinus rhythm with pronestyl. The transaminase values were 76 units on December 2, 1955 and 54 units on December 4, 1955. She was moderately febrile for 60 hours. Treatment consisted of digitalis, pronestyl, oxygen, sedation, narcotics, penicillin, and dicumarol. The hospital course was uneventful, and she was discharged without symptoms on January 12.

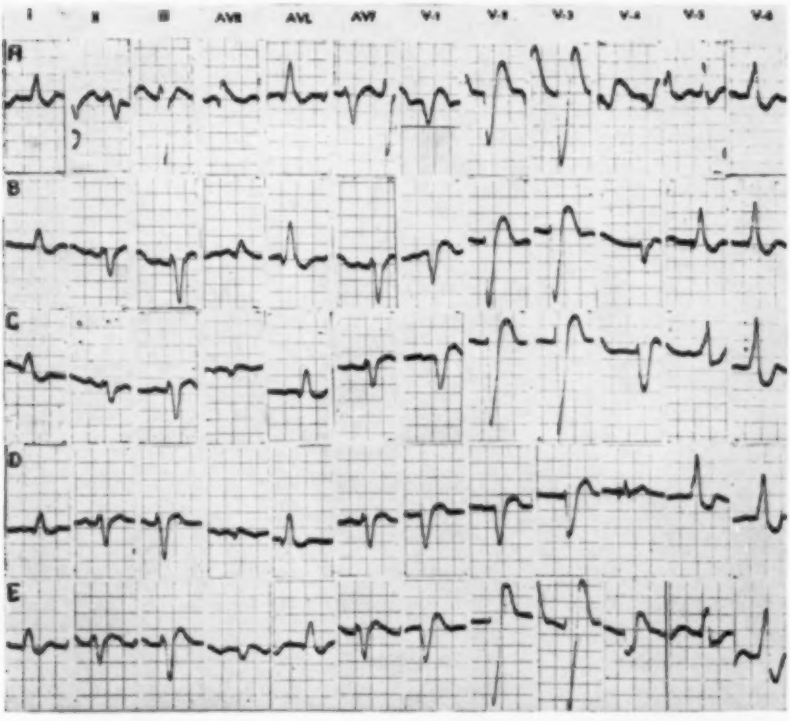


FIGURE 4: Left bundle branch block in all tracings. Tracing B—Shows a tiny Q wave in V5 and V6. Tracing C—Q wave is seen well in lead one. These changes though suggestive were not diagnostic of recent myocardial infarction. However, the elevated serum transaminase values proved that this had occurred.

4. An elevated serum transaminase may help establish the diagnosis of acute myocardial infarction in the presence of left bundle branch block.

Electrocardiographers find it difficult to make the diagnosis of acute myocardial infarction in the presence of left bundle branch block. The presence of elevated serum transaminase levels help us decide which of our patients with left bundle branch block have had recent myocardial injury.[12]

*Case 4:** A. R., a 75 year old white man was admitted to the hospital on September 11, 1955 with a long history of coronary artery disease. Ten years previously he had experienced his first attack of acute myocardial infarction with good recovery. He had no further acute distress until about a week prior to his present hospitalization, when he suddenly became dyspneic, began to cough, and developed some ankle edema. On the morning of admission he developed acute and severe chest pain which was not relieved by 150 mg. of demerol. On physical examination he was cyanotic and orthopneic. Blood pressure was 90/60. Head and neck showed no abnormalities. His chest was filled with rales. The heart tones were distant; there were frequent premature beats, and the apical rate was 110 per minute. His liver was palpable to three fingers below the costal margin, and there was 2+ pitting edema of both ankles. Neurological examination was normal. On admission the blood sugar was 125 mg./100 ml., N. P. N. was 40 mg./100 ml., and the icterus index was 5. The sedimentation rate was 11 mm./hour (corrected), hemoglobin 11.5 gm./100 ml., red blood cells 3.5 million/cu.mm., and white blood cell count 6,600/cu.mm. with a normal differential. Urinalysis was negative for albumin and sugar. X-ray film of the chest on September 12, 1955 (portable) revealed cardiac enlargement and congestion of the pulmonary vessels of both lung fields. A review of the electrocardiograms (Figure 4) shows the presence of left bundle branch

*Case 4 previously reported in the *Journal of the American Medical Association.*

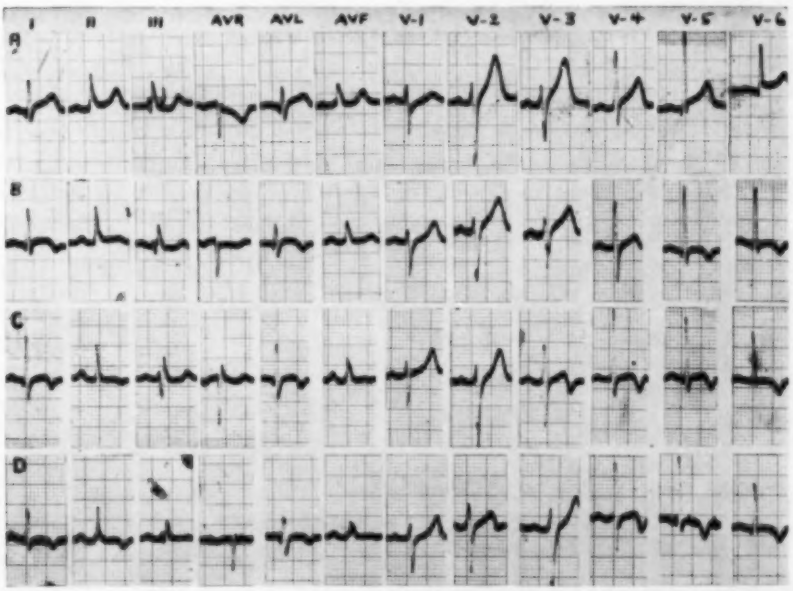


FIGURE 5: Tracing A—ST segment elevated in V5 and V6. Tracing B—T inverted in lead one, flattened in lead 2 and inverted in AVL, V5 and V6. Tracing C—T wave now also inverted in V3 and V4. Tracing D—T inverted in leads 1 and 2, AVL, V4, V5, and V6. These electrocardiographic changes are consistent with pericarditis. However, in view of the transaminase values the diagnosis of recent myocardial injury is warranted.

block in all tracings. In the tracing of September 11, 1955 there appears a tiny q-wave in the left ventricular leads which suggests recent myocardial infarction. A similar q-wave is seen in lead one in most of the series and is best seen in the tracing taken on September 15, 1955. The transaminase determinations were 120 units on September 12, 1955, 46 units on December 13, 1955, 60 units on December 14, 1955, and 68 units on December 15, 1955. Unfortunately no further transaminase determinations were run on this patient after September 15, 1955. It is interesting to note that after the initial rise there was a fall to 46 units followed by a secondary rise which probably was indicative of extension of the infarct.

5. Serum transaminase may help differentiate a recent myocardial infarction for acute pericarditis.

Although much has been written on the clinical and electrocardiographic diagnosis of pericarditis and its differentiation from myocardial infarction, there are always many cases which will be difficult to distinguish. The electrocardiogram, as in other instances of chest discomfort, is usually considered the final judge in ruling myocardial infarction "in" or "out." The serum transaminase determination now offers collateral evidence to reinforce our clinical and electrocardiographic interpretations.

*Case 5:* W. C., a 37 year old white salesman with a history of watery stools for three days was awakened the night of January 8, 1956 with nausea and moderately severe chest pain radiating to the left arm, but no sweating. The pain was felt over the entire left anterior chest and was accentuated with breathing. It disappeared, only to recur the following night when it persisted, and he was admitted to the hospital. He was in no distress but had already had morphine for pain. The blood pressure was 120/100. The sedimentation rate on January 12 was 15 mm/hour and on January 18, 30 mm/hour. The chest x-ray film demonstrated a patchy infiltration and linear scarring at both bases and a normal cardiac silhouette. Serum transaminase values were 150 units on January 12, 1956 and 80 on January 13, 1956. During his hospitalization he had two mild episodes of substernal pain, but was afebrile. Treatment consisted of oxygen, sedation, narcotics, heparin, dicumarol, and vitamins. He was discharged on January 23, 1956 without symptoms. Electrocardiograms (Figure 5) do not show any q-waves or ST deviation. The primary changes seen are in the T-wave, and the electrocardiographic diagnosis was "consistent with pericarditis." In view of the elevated transaminase values, however, the diagnosis of recent myocardial injury seems warranted.

6. Serum transaminase determinations may be helpful in clarifying the presence or absence of acute myocardial infarction, in the presence of digitalis "effects" in the electrocardiogram.

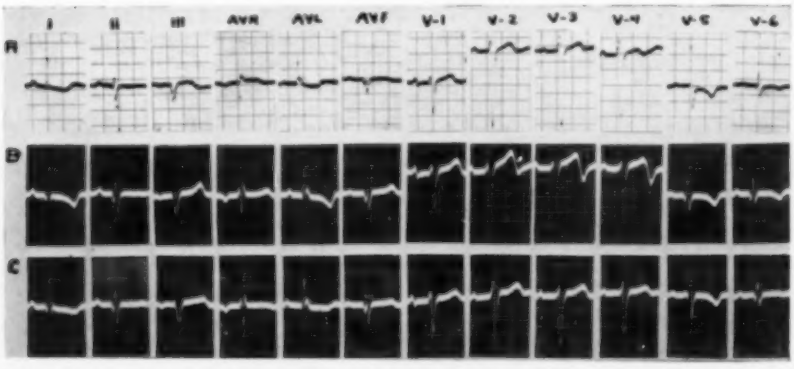


FIGURE 6: Tracing A—T wave inverted in lead one, AVL, V4, V5, and V6. Tracing B—T wave more deeply inverted in lead one, AVL, and now also inverted diphasic in V2 and V3. Tracing C—Similar to Tracing A with normal transaminase values. Acute myocardial infarction was excluded because of the normal transaminase values.

Since the electrocardiographic changes due to digitalis may resemble those of recent myocardial infarction, transaminase determinations may clarify this problem.

*Case 6:* A. M., a 59 year old white man was hospitalized January 23, 1956 with the chief complaint of chest pain. During the previous 14 months he had frequently experienced retrosternal pain upon exertion, with prompt relief by rest. During a previous admission, congestive failure had been successfully treated by the use of digitalis, diuretics and low sodium diet. Shortly after discharge, he discontinued this regimen and took no digitalis after January 7, 1956. On January 22, while at rest, he experienced severe pain to the left of the sternum of three hours duration accompanied by sweating. His leukocyte count was normal. Sedimentation rate varied between 10 and 12 mm/hour. A trace of C-reactive protein was detected on two separate serum samples. The initial transaminase determination was normal. His temperature remained normal. The electrocardiogram taken January 24 (Figure 6), revealed ST and T changes which had not been present one month previously. During the first three weeks of hospitalization serial electrocardiograms showed no significant change. Digitalis was restarted February 16. An electrocardiogram taken five days later revealed ST and T wave changes much less suggestive of recent myocardial damage, and this tracing resembled the electrocardiogram taken December 24, 1955. When digitalis was discontinued, ST and T waves became more abnormal, and superimposed upon previous QRS abnormalities suggested the possibility of recent myocardial infarction. Redigitalization reversed these ST and T wave changes. Normal transaminase levels, 12 units on January 25, 20 on January 26, 40 on January 27, and 24 on January 28, provided further evidence that he had not experienced an acute myocardial infarction.

7. An elevated serum transaminase level may confirm the diagnosis of a recent myocardial infarction superimposed on an old one.

It is quite common to have electrocardiographic evidence of myocardial scars following infarction. These findings, which might include deep and wide Q waves, absent R waves, ST deviations, and altered T waves, require serial electrocardiograms to determine their stability. Furthermore, it is possible for recent myocardial infarction to be concealed among these residual electrocardiographic deviations. Under these circumstances an ele-

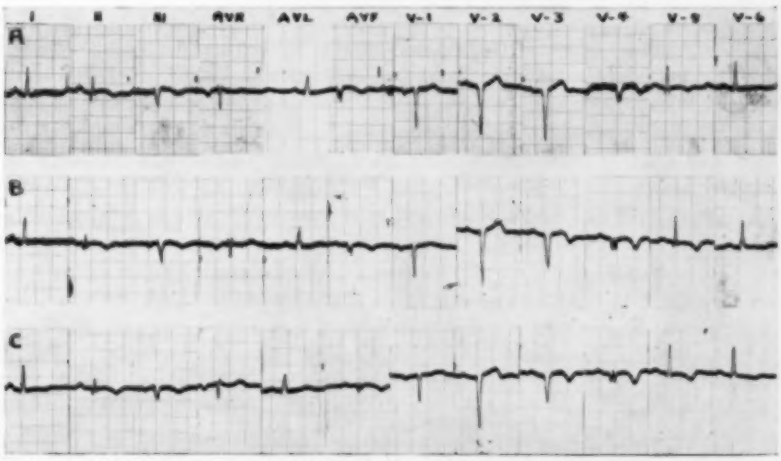


FIGURE 7: Tracing A—Q wave in lead 2. QS in lead AVF; T inverted in lead 2, lead 3 and AVF. Absent R wave in V1, V2, V3, V4, and T inverted in V5 and flat in V6. Tracing B and Tracing C—Show minor deviations from Tracing A. Even though there were only minor changes in these tracings the elevated serum transaminase values confirmed the clinical impression of recent myocardial infarction.

vated serum transaminase will be diagnostic for recent myocardial infarction, as demonstrated in the following case.

*Case 7:* This man of 44 years, was admitted to the hospital on June 20, 1956. He gave a history of having had a myocardial infarction in October 1953. He admitted to considerable angina and dyspnea with effort over the three years subsequent to the acute episode. In the week prior to admission he had been particularly uncomfortable with substernal and parasternal chest pain, radiating into his left arm. At noon on the day of admission this pain had become quite intense and persisted in spite of ¼ gr. of morphine sulfate. There was no abdominal symptom, no vomiting, or sweating. The family history was significant in that he had a 46 year old brother with coronary artery disease. Physical examination revealed small pupils that reacted to light and accommodation. Head and neck were negative. On examination of the heart $A_2$ was equal to $P_2$; the heart rate was slow and regular, and there was no significant murmur audible. The chest was clear to percussion and auscultation. Blood pressure was 90/60 in both arms. On June 21, the sedimentation rate was 15 mm/hour. Red blood count was 5.1 million/cu.mm., hemoglobin 15.5 Gm. per cent, white blood count 13,000/cu.mm., serum transaminase 74 units, blood sugar 118 mg./100 ml., N. P. N. 33.5 mg./100 ml., blood uric acid 7.6 mg./100 ml., and serum cholesterol 305 mg./100 ml. On June 20, 1956 the serum transaminase was 78 units; this dropped to 40 two days later. The chest pain gradually subsided and the remainder of his hospital course was uneventful. The serial electrocardiograms (Figure 7) reveal evidence of the old myocardial infarction, but at no time was there indication of the recent episode.

## SUMMARY

The determination of the level of transaminase activity in the serum should not be used to replace the electrocardiogram, but to supplement it. It is of value when the diagnosis of acute myocardial infarction is suspected clinically but cannot be confirmed electrocardiographically. This situation frequently arises when a history suggestive of an acute coronary occlusion is obtained and the electrocardiogram is recorded too early for changes to appear. Or, the electrocardiogram, though abnormal, may not be completely diagnostic of recent myocardial injury but exhibits equivocal changes usually consisting of minor ST deviations or T wave inversions. Severe chest pain, particularly that following an operative procedure, will raise the question of a differential diagnosis between acute pulmonary embolism or an acute coronary occlusion and neither the electrocardiogram nor chest x-ray film may be helpful in arriving at a decision. An elevated serum transaminase level, however, will clarify the issue by shifting the evidence in favor of the latter. Not uncommonly the electrocardiographer is confronted with a tracing that shows the pattern of left bundle branch block when acute myocardial infarction is suspected. Since conduction defects of this type can obscure the electrical signs of recent myocardial injury, the presence of an elevated serum transaminase level may prove of value. Another application of this laboratory test is in the identification of recent myocardial injury superimposed on the residual signs of old cardiac damage—a situation which may "neutralize" the characteristic changes produced by injury currents. The early appearance of an elevated serum transaminase value can confirm the clinical impression of additional myocardial damage. Also, serial serum transaminase determinations may help confirm or rule out recent myocardial damage when the electrocardiographic interpretation is complicated by an arrhythmia such as ventricular tachycardia where the contour resembles that of a recent infarct. Serial determination of the serum transaminase activity may also be of consider-

able value in assisting one to distinguish the electrocardiographic pattern of myocardial infarction from that of pericarditis or digitalis effect. Thus, we are of the opinion if serum transaminase levels are obtained early enough, and in a serial fashion following suspected myocardial infarction, a normal value is just as important in ruling out the presence of this lesion as an elevated value is in confirming the clinical impression.

RESUMEN

La determinación del grado de actividad de la transaminasa en el suero no debe ser usado en substitución del electrocardiograma sino debe ser un suplemento de éste. Es de valor cuando el diagnóstico de infarto cardiaco agudo se sospechá clínicamente, pero no puede ser confirmado electrocardiográficamente. Esto se presenta frecuentemente cuando se obtiene una historia sugestiva de oclusión coronaria ye es muy pronto para que haya cambios electrocardiográficos, o bien el electrocardiograma normal, puede no ser completamente diagnóstico de reciente daño del miocardio sino que muestra signos equívocos que consisten generalmente en desviaciones menores de ST o inversiones de la onda T.

El dolor intenso del pecho, especialmente después de una operación, puede plantear el problema del diagnóstico diferencial entre embolia pulmonar aguda o una oclusión coronaria aguda y ni el electrocardiograma ni la radiografía de tórax peuden ser útiles para llegar a una decisión.

Un nivel elevado de transaminasa en el suero, sin embargo, aclarará el caso por la desviación en favor de la segunda.

No es poco común que el electrocardiografista se enfrente a trazos que muestren aspecto de bloqueo de rama izquierda cuando se sospecha infarto agudo del miocardio. Puesto que los defectos de conducción de este tipo pueden obscurecer los signos eléctricos de daño reciente del miocardio, la presencia de transaminasa elevada puede ser de valor. Otra aplicación de esta prueba de laboratorio es la identificación de daño reciente del miocardio sobrepuesto a signos residuales de antiguo daño cardiaco—situación que puede "neutralizar" los cambios característicos producidos por las lesiones actuales. La aparición temprana, de una transaminasa elevada en el suero puede confirmar la impresión clínica de daño miocárdico adicional. Además las determinaciones en serie pueden ayudar para confirmar o descartar los daños miocárdicos recientes cuando la interpretación del ECG es complicada por una arritmia tal como la taquicardia ventricular en la que el trazo se parece al de un infarto reciente.

La determinación de la transaminasa n serie puede ser también de considerable valor para distinguir el trazo del infarto del miocardio del de la pericarditis o del efecto digitálico. Así, somos de opinión que si la transaminasa se determina bastante tempranamente y en series cuando se sospecha lesión miocárdica un valor normal es tan importante para descartar la presencia de esta lesión como un elevado tenor sirve para confirmar la impresión clínica.

RESUME

La détermination du taux de l'activité transaminasique du sérum ne doit pas remplacer l'électrocardiogramme mais le compléter. C'est un procédé de valeur lorsque la clinique fait soupçonner le diagnostic d'infarctus aigu du myocarde et que l'électrocardiogramme ne semble pas le confirmer. Cette situation survient fréquemment lorsqu'on est en présence d'une histoire évocatrice d'une occlusion coronarienne aiguë, et que l'électrocardiogramme est enregistré trop précocément pour que des modifications apparaissent. Ou encore lorsque l'électrocardiogramme bien qu'anormal, ne permet pas d'affirmer nettement le diagnostic de trouble myocardique récent, mais montre simplement des altérations suspectes consistant ordinairement en déviations ST mineures ou en inversions de l'onde T. Une douleur thoracique sévère, particulièrement lorsqu'elle suit l'intervention chirurgicale, soulèvera la question du diagnostic différentiel entre embolie pulmonaire et occlusion coronarienne aiguë, l'électrocardiogramme ou le cliché thoracique ne peuvent être d'une grande utilité pour permettre de conclure. Un taux élevé de transaminase dans le sérum cependant éclairera la question en faisant pencher la balance en faveur de la seconde hypothèse. Il n'est pas rare que l'électrocardiographe présente un tracé de bloc de branche gauche, quand l'infarctus myocardique est suspecté. Alors que les défauts de conduction de ce type peuvent masquer les signes électriques d'une atteinte myocardique récente, la présence d'un taux élevé de transaminase du sérum peut se révéler de grande valeur. Une autre application de ce test de laboratoire est précieuse dans l'identification d'un trouble myocardique récent surajouté aux signes résiduels d'une altération cardiaque ancienne, situation qui peut "neutraliser" les altérations caractéristiques d'une atteinte myocardique. L'apparition précoce d'un taux élevé de transaminase du sérum confirme l'impression clinique d'une altération myocardique surajoutée. Aussi, la recherche en série des taux de la transaminase du sérum peut-elle aider à confirmer ou à infirmer une altération myocardique lorsque l'interprétation électrocardiographique est compliquée d'une arythmie, telle que la tachycardie ventriculaire, dont le tracé ressemble à celui d'un infarctus récent. La recherche en série du taux de transaminase peut aussi être d'un grand intérêt en aidant à distinguer la courbe électrocardiographique de l'infarctus myocardique de celle de la péricardite ou de l'effet digitalinique. C'est pourquoi les auteurs pensent que si les taux de transaminase du sérum sont connus suffisamment tôt, dans une série d'examens suivant une suspiscion d'infarctus myocardique, la constatation d'une taux normal est aussi importante pour éliminer la possibilité de cette lésion que la constatation d'un taux élevé pour confirmer l'impression clinique.

ZUSAMMENFASSUNG

Die Feststellung des Ausmasses der Transaminase-Aktivität im Serum sollte nicht benutzt werden, um das Elektrocardiogramm zu ersetzen, sondern um es zu ergänzen. Sie ist von Wert, wenn die Diagnose eines akuten Myocard-Infarktes klinisch vermutet wird, sich aber elektrocardiographisch nicht bestätigen lässt. Diese Situation tritt häufig ein, wenn man

in einer Vorgeschichte auf den Verdacht eines akuten Coronarverschlusses stösst und das Elektrocardiogramm zu früh aufgenommen wird, als dass schon Veränderungen erscheinen könnten, oder das Elektrocardiogramm, obwohl es verändert ist, keine vollständige Diagnose eines frischen Myocardschadens ergibt, sondern verdächtige Veränderungen, die gewöhnlich in geringeren ST-Abweichungen oder T-Zacken-Umkehrungen bestehen. Stärkerer Brustschmerz, besonders wenn er sich an einen operativen Eingriff anschliesst, lässt, die Frage entstehen nach der Differentialdiagnose zwischen einer akuten Lungenembolie oder einem akuten Coronarverschluss, und weder das Elektrocardiogramm, noch eine Thorax-Röntgenaufnahme ist zur Hilfe imstande, wenn man zur Entscheidung kommt. Eine Erhöhung des Serum-Transaminase-Spiegels kann jedoch dem Sachverhalt klären durch Verlagerung des Beweismaterials zu Gunsten des letzteren. Nicht selten steht der Arzt mit seinem Elektrocardiogramm einem Befund gegenüber, der dem Typ eines linksseitigen Schenkelblocks entspricht, während er den Verdacht auf einen akuten Myocard-Infarkt hegt. Wen also Ableitungsstörungen dieser Art die elektrischen Zeichen eines frischen Myokard-Schadens verwischen können, so kann sich das Vorliegen eines erhöhten Serum-Transaminase-Spiegel als von Wert erweisen. Eine andere Anwendung dieses Laboratorium-Testes besteht in der Erkennung frischer Myocardschädigungen, die such den restierenden Zeichen eines alten Herzschadens aufpfropfen;—eine Situation, die die für die die Schädigung anzeigenden Ströme charakteristischen Veränderungen "neutralisieren" kann. Das frühe Auftreten eines erhöhten Serum-Transaminase-Wertes kann den klinischen Eindruck eines zusätzlichen Myocard-Schadens bestätigen. Darüber hinaus können serienmässige Transaminase-Bestimmungen dazu beitragen, eine frische Myocard-Schädigung entweder zu bestätigen oder auszuschliessen, falls die elektrocardiographische Auswertung kompliziert ist durch eine Arrhythmie bzw. vetriculäre Tachycardie, wo die Befunde denen eines frischen Infarktes ähnlich sehen. Serienmässige Bestimmungen der Serum-Transaminase-Aktivität kann schliesslich auch von beträchtlichem Wert sein als Beistand bei der Unterscheidung der elektrocardiographischen Veränderungen der Myocard-Infarkt-Bildung von denen einer Pericarditis oder einem Digitalis-Effekt. Wir vertreten somit die Meinung, dass, wenn Serum-Transaminase-Werte frühzeitig genug erhoben werden und in serienmässiger Weise im Anschluss an eine verdächtige Myocard-Infarktbildung, ein normaler Wert ebenso wichtig ist zum Ausschluss des Vorliegens dieser Varänderung wie ein erhöhter Wert es ist zur Bestätitgung dieses klinischen Eindrucks.

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# Surgical Treatment of Pulmonary Tuberculosis

THOMAS J. KINSELLA, M.D., F.C.C.P.
Minneapolis, Minnesota

No field of medicine or surgery has undergone more drastic changes in the past decade than has the treatment of pulmonary tuberculosis. The modern treatment of this disease bears so little resemblance to that so generally accepted a few years ago that anyone trained in the earlier tuberculosis program but out of touch with the field for the past several years would be almost totally lost; a stranger in a strange land in today's program. Gone are the sleeping porches, the sundecks, the backyard shacks, the postural rest, the compression jackets, the heating pads and the stone hot water pigs as well as many of the sanatoria which were so crowded with health seekers not so many years ago.

Bedrest, prolonged and intensive, has been replaced by a very modified type of rest program, or none at all, plus intensive antimicrobial therapy. The old dictum of Sir William Ostler, "In tuberculosis we prescribe not drugs but a mode of life," has now been almost reversed. Surgery of a somewhat hesitating and indirect type has given way to an aggressive definitive attack. The phthisiologist of yore who formerly boasted that he protected his patients from the attacks of the surgeon has now been displaced by one whose zeal for surgical treatment must, not infrequently, be tempered and restrained by some of his more conservative surgical brethren.

The idea behind all of this is not new. The dictum of Lady Macbeth, "Out damned spot," has long had a strong appeal to the surgeon phthisiologist. Tuffier in 1891 successfully excised a tuberculous area from the apex of the lung. Subsequently, his experience and that of other surgeons who followed the same attack proved the procedure to be too costly. It is only because of modern developments in chemotherapy, anesthesia, blood banks and transfusion techniques, oxygen therapy and a better understanding of segmental anatomy of the lung and surgical techniques that the present program has become possible.

There can be no denying that many of the older forms of therapy were extremely valuable and that they contributed much to the control of tuberculosis over many years. There are thousands of people in good health today as living proof of the value of many of the procedures now abandoned. They are no longer in extensive use only because we now feel that we have something better to offer.

## *Pneumothorax*

Pneumothorax, once the stand-by and lifesaver for many who did not improve under bedrest alone, has now largely been abandoned in most sections of the country. The extent to which this has occurred is well illustrated by the fact that one large sanatorium which at one time carried more than 50 per cent of its patients under this form of therapy now has only a

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scattering of hold-overs. In my own office practice which listed 136 pneumothorax patients in 1944, I now have only four. But did the procedure deserve such a fate?

True, there were disadvantages and complications to its use but many of them were man-made and altogether avoidable. Poor technique and poorer judgment not infrequently clouded the pneumothorax picture and greatly influenced the results and complications. Many were pushed too far, carried too long and many more not abandoned soon enough. Complications were not infrequent, many of them avoidable but some, such as empyema, became serious and required other types of treatment. Yet many patients who could not have survived without it because they were absolutely unsuitable for any other type of treatment lived and recovered because of the pneumothorax.

With antimicrobial therapy of tuberculosis, the majority of the indications for artificial pneumothorax have disappeared. Under chemotherapy, I am sure that many of the effusions, the empyemas and other complications that were encountered during pneumothorax treatment would not have occurred. While I am not advocating a return to the older times, I wonder if even today there may not be a time or a place for chemotherapy plus pneumothorax, especially in the aged and infirm and some of the patients who are exceptionally poor risks for any major surgical procedure. Perhaps even in some of this group the thoracoscope and closed intrapleural pneumonolysis might even be resurrected.

*Decortication*

We still see a few patients who have recovered from tuberculosis who must continue to carry a pneumothorax pocket for many years after the tuberculosis has been controlled for the simple reason that the lung has become bound down and will not expand because of a condensate of fibrin on the pleural surface. Any attempt to discontinue the pneumothorax results in high intrapleural negative pressure followed by pleural effusion with more fibrin deposit. Attempts to expand the lung without decortication not infrequently results in a disruptive over-distention of local segments with harmful bleb formation. Decortication may enable the lung to expand and fill the pleural cavity. The facility with which this can be accomplished is determined not so much by the duration of the pneumothorax collapse as by the intensity of the inflammatory reaction in the lung and on the pleura. Some are accomplished readily, others are extremely difficult and some are impossible.

Preliminary studies by bronchoscopy, bronchography and bronchospirometry as well as a review of the original x-ray films should give a definite idea as to the possibilities of future function of the re-expanding lung. It is well to remember that extensive tuberculosis and its healing takes with it its blood supply, and that not a few of the re-expanded lungs may be more valuable as a space filler than as a functioning breathing organ.

The lung bound down by primary pleural effusion, on the other hand, frequently contains little parenchymal disease. The lung entrapped by the exudate of chronic empyema of some duration is not infrequently more

difficult to decorticate and expand but this does not necessarily follow. The functional result obtained likewise is variable, depending upon the amount of original disease present in the lung. By and large, it is a procedure of distinct value but not always as easily accomplished as some of our medical confreres would assume. Not infrequently in the patient who has had considerable disease in the lung, decortication must be combined with resection of a significant residual disease. In such a case, difficulty may be encountered in obliteration of the pleural cavity and a tailoring thoracoplasty required to obliterate the space.

### *Pneumoperitoneum*

Pneumoperitoneum, never as popular or as effective as pneumothorax, has likewise almost disappeared from the scene as chemotherapy has taken care of many of the situations in which it was used. It might still be remembered for some patient when the going is particularly rough even under chemotherapy.

### *Phrenic Nerve Surgery*

Interruption of the nerve supply to the hemidiaphragm, once so popular as to be almost a routine procedure in some areas, has now fortunately almost been forgotten. It was always somewhat overrated as a therapeutic procedure. It did have the disadvantage of seriously impairing the function of the most valuable of all respiratory muscles, the diaphragm. We are still confronted with patients whose respiratory function has been seriously reduced and in whom future definitive surgery has been seriously compromised by previous injudicious phrenic nerve surgery. May it never come back into popular use.

### *Plomage and the Extrapleural Operations*

The siren song of the extrapleural operation lured many a surgeon, present company not excepted, into error and many a patient into late troubles at a time when he thought he was well out of the woods and rehabilitated. The attractions were many. There was little shock, maximum collapse with minimal trauma, conservation of breathing space and one operation instead of three. All of these had a sweet seductive appeal. The procedure did not need to be sold to the patients; they begged for it and many patients were so treated and many gratifying results were obtained temporarily. The patients recovered, were discharged and apparently rehabilitated. Then things began to happen. As Ralph Mattson said many years ago concerning his oleothoraces, "It was nice while it lasted but after four or five years, they all blew up."

The earlier complications had been conquered by changes in technique and subsequently by chemotherapy but the late complications began to crop up at the most inopportune time. It might be three, five, or even seven or eight years later but things began to happen. It made little difference whether the extrapleural plombage was air, oil, paraffin or wax, lucite spheres, ivalon, cellophane or polythene, the space was just too close to the lung and infection, perforation, migration and protrusion or extrusion

came into the picture. The body reacted unfavorably to any foreign material over a period of time and tried to get rid of it.

We were guilty of this error like many others many years ago and did more than 65 of these procedures over a five year period from 1934 to 1939. For five long years, aside from a few early complications, we were happy in our blissful ignorance and could truthfully say that we had seen no perforation, migration, extrusion or late infection in any of these patients. Then things began to happen and they are still happening to these patients. Now 15 to 22 years later, there are not over a half dozen of these patients who are still carrying their packs and have not gotten into trouble. Just when the patient had been rehabilitated, apparently settled and established with family and business responsibilities, he was again in trouble of man-made etiology.

Later, the extraperiosteal type of plombage came into the picture. It was farther away from the lung, the blood supply was better and therefore it should be better. Subsequently, paraffin, lucite, ivalon, cellophane and polythene were all used with results which were quite gratifying on a temporary basis. Time and the law of averages has already recalled to some that even in this antibiotic age, the tissues of the body will not indefinitely tolerate the presence of foreign material. It should be a moral if not a legal requirement that any surgeon undertaking such procedures be required to live and remain on service for a sufficient period of time that he may correct or undo the troubles which he has created.

### *Thoracoplasty*

Extrapleural thoracoplasty, once the last resort procedure when all else had failed, was yet the saviour of countless thousands of individuals with extensive pulmonary tuberculosis. In spite of this, it has likewise been relegated to the background in many parts of the country. Used as it once was in many otherwise hopeless and not a few impossible situations, it proved its worth over many years.

With experience, it became evident that certain types of lesions were not suitable for thoracoplasty and did not respond to it. Good results did not occur in fresh exudative tuberculosis, in incompletely excavated cavities, in isolated solid lesions, in the presence of bronchial obstruction with balloon cavity and many lower lobe lesions and in lower lobe bronchiectasis. Such conditions accounted for many of the thoracoplasty "failures." Considering the type of material submitted for thoracoplasty, the risk of the surgery was not particularly great. We reported, from 1941 to 1943, a consecutive series of 240 thoracoplasty operations with no deaths within eight weeks of the surgery and subsequently, from February, 1947 until May, 1951, Drs. Funk and Larson at Glen Lake Sanatorium had a consecutive series of 752 thoracoplasty operations without any operative deaths under two months. Once a patient obtained a good result from a thoracoplasty operation, that result was usually permanent and there were few, if any, late complications of the procedure. The facts that multiple stage procedures were frequently required and that much good pulmonary tissue must be sacrificed in order

to collapse the cavitary area were the greatest arguments against thoracoplasty.

The results from thoracoplasty treatment were good. From a series of 613 patients treated by thoracoplasty at Glen Lake Sanatorium from 1922 to 1943, sputum conversion by the smear and concentrate technique was obtained in 88.1 per cent of the patients. Unquestionably, our present criteria of negativity by culture of sputum or gastric contents are much more exacting and would have materially reduced this percentage. Closure of large cavities (more than 4 cm. in diameter) occurred in 49.6 per cent with sputum conversion in 76.5 per cent. Small cavities (under 4 cm. in diameter) showed 68.7 per cent closure and 91 per cent sputum conversions. These figures were, of course, without planigraphic studies which were not available at that time. It is well to remember that all of these figures are reported from an era before there was any chemotherapy or antimicrobial therapy. With antibiotics available, thoracoplasty today could give infinitely better results than those heretofore reported. Thoracoplasty today I believe might be used to good advantage in many situations, particularly in certain areas where the mortality and morbidity from resectional therapy is still high.

*Resectional Therapy*

Modern resectional therapy has been made possible by a number of factors which have contributed greatly to the technical and safety factors of the procedure. Without any one of these, the whole picture would be changed unfavorably. We need waste no time in arguing which is the most important or which has contributed the most toward making this program possible. May it be said only that without any one of the group, our work would be definitely more difficult and certainly more hazardous.

Resectional treatment of pulmonary tuberculosis has already established itself as a great step forward in our treatment of this disease. As it is still in the developmental stage as it were, an exact statement of its limitations and contraindications as well as its indications cannot be settled. The questions of how soon or how late, how little or how much and many other factors are still to be determined. In order to try to evaluate the position of resectional therapy as compared to other types of therapy, we must split the indications into several categories.

*I. Thoracoplasty failures:* These patients fall into a variety of groups.

1. Those in whom thoracoplasty failed to close a cavity.
2. Those in whom the cavity is apparently closed but subsequently re-opened even many years later.
3. Those with apparent cavity closure according to all studies but with a positive sputum.
4. Patients with an unobliterated empyema pocket.
5. Patients with apparent cavity closure and conversion of sputum but who are still left with cough and expectoration.
6. Patients in similar category without sputum but with profuse or recurrent pulmonary hemorrhage.

In 1936, we offered surgical revision of the unsatisfactory thoracoplasty with re-operation and extraperiosteal packing by plombage as a possible remedy for some of these conditions with results which at that time were quite favorable. The procedure, however, was prolonged and difficult, quite traumatic and distressing to the patient and quite time consuming and did not meet all of the problems presented, particularly that of lower lobe disease and residual bronchiectasis. These patients require careful study to determine the presence and position of cavity, the status of the bronchus as to active tuberculous stricture or bronchiectasis, an evaluation of the cardiovascular system and the vital and functional capacity of the remaining lung or lobes.

Pulmonary resection offers a far better answer to the problems presented than the previous re-operation revision technique and offers a shorter and more certain means of accomplishing a good result.

*III. Bronchiectasis:* Pulmonary tuberculosis in its healing presents two factors which favor the development of bronchiectasis in the involved lung. The intense fibrosis produced by the healing of tuberculosis and the bronchial strictures resulting from tuberculous bronchitis in its healing both lead to this end. If the bronchiectatic process be in the upper lobe and the amount of secretion not too great, the bronchiectasis may remain relatively asymptomatic because of the free drainage afforded the affected areas in the upright position. Bronchiectasis of the middle and lower lobes, however, is quite prone to cause trouble because of inadequate drainage. Thoracoplasty is not the cause of bronchiectasis in these patients though it may bring about aggravation of symptoms by angulation of the bronchi and by the production of atelectasis in the surrounding lung tissue which interferes with the cough effort. Thoracoplasty has notoriously failed to produce good results over the years in treating bronchiectasis. Resection of the involved segments or lobes, or even the entire lung, is an adequate answer to this problem.

*III. Pulmonary hemorrhage not due to active pulmonary tuberculosis:* Not infrequently, we are now confronted with patients who have recovered from tuberculosis who are negative for acid-fast bacilli on all types of tests including cultures in whom suddenly, apparently out of a clear sky, pulmonary hemorrhage occurs. Careful study fails to reveal any evidence of tumor or any uncollapsed cavity but will usually reveal an area of bronchiectatic dilatation either in the area of previous disease or in some other segment. Local excision of the involved segment or segments here produces excellent results.

*IV. Persistent cavitation after chemotherapy:*

Failure of cavitary areas to close and disappear following intensive chemotherapy for a period of four or five months should, I believe, call for consideration at least of the possibilities of resectional therapy to eliminate this open focus of disease even though the sputum be negative. If the sputum should still be positive either on smear or culture, the indications are all the more urgent that something definitive be done either in altering

chemotherapy or directly attacking the open focus or preferably both. It is in this situation that bacterial resistance of the drugs in use develops most rapidly and most frequently. The addition of a third drug for a short period of time, say a few weeks, followed by removal of the uncollapsed cavity will frequently give a good result with less hazard than if chemotherapy is continued indefinitely and the organisms become resistant to all the drugs. If, because of extent of disease or other factors, resection does not seem advisable in this situation, local collapse therapy in an attempt to bring about closure of the cavity might well be instituted and the resection held in abeyance until a more favorable time.

*V. Persistent significant disease, residual after intensive chemotherapy:* The modern intensive chemotherapeutic treatment of pulmonary tuberculosis to the point of maximum clearing of the inflammatory process (target point) has been fairly generally accepted in principle, the difference of opinion arising concerning what is maximum improvement, what is target point and what is a significant residual amount of disease. From our standpoint, if the improvement shown on monthly x-ray films has slowed to a crawl or is measured in only millimeters, there is usually little to be gained and considerable time and money to be lost by an additional waiting period. More waiting does not, as a rule, enable the surgeon to save more good lung tissue and adds nothing to the safety of the procedure but does add to the total cost to the patient or the community. I feel that if the same total amount of treatment time is to be expended, it is much better to invest more of it post-operatively and in rehabilitation.

The question as to what constitutes significant residual disease is a big one. If the residual is large and dense and the segment or lobes atelectatic, bronchiectatic or cavitary, there is no doubt about it. The question comes in the smaller lesions. There is little virtue and certainly less satisfaction in the excision of fibrotic scars or fibrotic tubercles of one or two millimeters in diameter, but there is much value and satisfaction in the removal of "garbage" (Medlar) in the form of cavity, inspissated cavity, caseous abscesses, atelectatic and bronchiectatic areas and larger nodules or conglomerate areas of nodular disease. Just where the line should be drawn or how this information can be obtained is a serious question. X-ray films of the chest, planigraphic studies in antero-posterior or lateral projections, culture studies, and more particularly, a careful review of the original lesion and its changes during treatment most frequently give the clue to the nature of the possible residues. Though they are notoriously somewhat inaccurate, they are the best we have to offer.

All surgeons have had the experience of discovering areas of unsuspected disease, caseous abscesses where fibrotic scars were anticipated, cavities not demonstrated previously and no cavities where the planigraphic studies apparently revealed areas of excavation, and very frequently, numerous small to medium sized nodules in areas previously thought to be free of disease. Some of the westerners say, "only fools and tourists predict the weather," and so the experienced surgeon rarely predicts what he is going to encounter, but humbly proceeds to take care of the situation as it pre-

sents itself.

The big question is how dangerous are the residual caseous areas medium to small in size that is, under one centimeter in diameter, to the future of the patient, particularly under prolonged antibiotic therapy? Certainly in the older days, many lesions of this size and larger went on to encapsulation under collapse therapy and some to eventual healing as evidenced by the prolonged good results in many of our pneumothorax and thoracoplasty patients. Just how many will do so and which lesions will do so is as yet undetermined. We know how much we can remove surgically, but we do not know how much disease we can leave in safely. On the other side of the picture is the report of the pathologist. The microscopic picture of many of these resected lesions shows considerable pathological activity in the wall and, not infrequently, acid-fast bacilli in the caseous material even though cultures from much of this material are negative during the ordinary time of observation, particularly with the patient under chemotherapy. The unhappy thought remains that it was the unhealed caseous lesion of similar type which, in days gone by, accounted for the reactivation and spread of tuberculosis in many patients.

The numerous vacant beds in our sanatoria are largely the result of shorter periods of treatment and a marked reduction in the number of readmissions of patients who have undergone relapse of their disease. Let us continue to keep it so and treat our patients intensively and adequately for permanent results, not merely temporary improvement. When, after all pertinent studies, I resect a residual lesion which turns out to be a rather innoxious process, I am disappointed but I am not distressed for I have not harmed the patient, and both the patient and I are very happy in the knowledge that this is good evidence of his ability to heal tuberculosis. We are given greater assurance that he will attain a permanent result.

*VI. Bilateral disease:*

Resectional therapy, in contrast to collapse therapy, not infrequently offers a conservative approach to the treatment of bilateral disease for it permits us to excise local areas of disease, notably the apical segment or apical and posterior segments or these two plus the superior segment of the lower lobe and at the same time, to conserve the remainder of the lung to fill the chest and to function subsequently. Collapse therapy procedures on the contrary, not infrequently immobilize or destroy the function of large areas of healthy lung tissue with the involved area. As the patient's working capacity is intimately associated with his functional vital capacity, these considerations become increasingly important in the patient afflicted with bilateral disease. Bilateral pulmonary resections of varying degrees, depending upon local conditions, are best performed in sequence allowing time for recovery of vital capacity between stages. May simultaneous bilateral pulmonary resection for tuberculosis, now that it has been reported, remain in the archives as a stunt once accomplished but presenting few indications for its repetition.

We are still seeing patients occasionally who present such extensive tuberculosis that no form of therapy save a true miracle could possibly elimi-

nate or control all of the disease. Some of these patients, from the very start of their disease, were doomed so far as recovery was concerned. Not a few of them come from some of the older small sanatoria which now have been closed and where the patients have been in residence for years without end. Some represent therapeutic failures of both omission or commission and some plain therapeutic blunders. Age, emphysema and intercurrent disease have added to their troubles and detracted from their therapeutic possibilities. Usually, they are sputum positive, hence a possible menace to those around them and they are therefore doomed to an institutional life for the rest of their days.

The patients' courage is frequently magnificent, their cooperation ideal, their eagerness and hope bordering on desperation and their confidence in the new treatments and the surgeon, in spite of past sad experiences, most edifying and yet embarrassing to one who knows the true score in their situation. We have inherited more than our share of such problems for, while the larger institutions have for a number of years been cleared of such problems, the closure of seven smaller institutions in the state has confronted us with a considerable group of such problems and their pleas are oftentimes pathetic. "We know that he is old, that he has heart disease, that he has emphysema, but can't you do something for the poor fellow, not necessarily to cure him, but can't we get him sputum negative so that we can discharge him from the sanatorium and back to his home if only for a few years?" Frequently, on top of all of the other things, the patient's organisms are resistant to every drug known to affect the tubercle bacillus. Occasionally even from this group, we get results which are most gratifying and heart-warming and present a thrill comparable to few things in this world. True the results are not many and the risks are great, but the rewards when they come are well worth it. Take for example just one patient who spent his entire life from the age of 17 to 45, a consecutive period of 28 years, in a sanatorium and yet, by resectional surgery, was rendered culture negative and returned to his home.

*Special groups: I. The aged:*

The average age of admission of patients to the sanatorium has increased gradually over the years from an average in the late teens or twenties in 1925 to a mean average age of 50 or above at the present time. Many, but not all, of these patients present chronic disease which does not respond rapidly or completely to chemotherapy. In addition, they present the old-age complications of arterioscelerosis, nephritis, hypertension, bronchitis, emphysema, bronchiectasis, urinary disease and diabetes to complicate the therapeutic picture, and not a few are confirmed alcoholics in the bargain. To render them sputum negative and non-infectious so that they do not have to be institutionalized all the rest of their life is the problem. Complete eradication of all disease is not frequently possible. A low vital capacity and many other factors limit the therapeutic possibilities. Physiological rather than attained age is frequently the important thing. The therapeutic aim in many of these must be to try to render the patient sputum negative

and non-infectious rather than to remove all disease so the resections must be held to a minimum for many reasons. No one can state categorically the top age limit for the patients who may be treated by resectional surgery for many conditions alter this picture. Some are far older at 50 than other patients are at 70. We know that many patients above 65 do not tolerate extensive resections, especially pneumonectomy, though there are occasional exceptions. The smaller resections and lobectomy may be well tolerated. Such resections in patients in the 70's have turned out well in carincoma and in some with tuberculosis. Each must present an individual problem. No patient must be rejected categorically just because he is old.

*II. Diabetics:*

The frequency of pulmonary tuberculosis among diabetics is not adequately appreciated by many internists and general practitioners, consequently, the diagnosis is frequently delayed and characteristically the disease is not often extensive and bizarre in nature. Before the days of chemotherapy, the combination was a bad one because the restricted food intake necessary to keep the diabetes in control not infrequently interfered with the healing of the tuberculous process. With chemotherapy and insulin, this handicap has been alleviated to a considerable degree. Not a few of the patients handle their tuberculosis relatively well though the tuberculosis complicates the handling of the diabetes to a considerable degree. Because of the location, intensity, nature and the extent of the disease, not a few of them are left with significant residual disease, cavitary or otherwise. Resectional surgery has proved a distinct boon to these patients. Working in conjunction with internists and phthisiologists, we have performed 50 resections on 40 diabetic patients carrying out three pneumonectomies, 16 lobectomies and 31 partial resections with one death (2 per cent). The mortality has been low, the complications few and the results surprisingly good. As one would expect, the control of the diabetes often became a simpler problem following the control of the tuberculosis.

*III. Indians:*

Minnesota has a problem with some 19,000 Indians, varying from full-bloods to the very dilute mixture, resident within the state. There are between 5,000 and 6,000 of these in the city of Minneapolis. Their economic status is not good. The incidence of tuberculosis in these people has been quite high. Our neighbor states of North and South Dakota, likewise, have a considerable Indian population with similar tuberculosis contamination. Not infrequently they have been subjected to a severe contamination with tuberculosis and present extensive disease. Added to that, their poor economic conditions, their restlessness and tendency to discontinue the cure at frequent and unpredictable intervals present a real problem in the therapeutics of tuberculosis. Many are Christian but some are still pagan. Some still believe in Big Medicine and want little to do with the White man's institutions and treatment. As a race, they have been lied to and cheated for generations and it takes time, careful handling and much kindness to gain their confidence. Their reactions many times are like those of children.

They come and go on the slightest provocation, one whom we have treated having her resection on her 30th readmission to the sanatorium.

Through the cooperation of the Minnesota State Sanatorium, the North Dakota State Sanatorium and the Sioux Sanatorium at Rapid City, South Dakota, we have had the opportunity to treat a considerable number of these patients with the resection series in this group now totaling 175 operations on 164 patients. Their ability to handle tuberculosis is equal to that of the Whites if poor nutrition, economic conditions, massive contamination and interrupted periods of treatment are all taken into consideration. The total mortality for this group has been 1.71 per cent with 52 lobectomies, 22 pneumonectomies and 101 partial resections.

The complications have been no greater than among the white patients and in general they have tolerated their surgery better than the Whites. It is not at all infrequent to bring the patients down by ambulance 200 miles on a Tuesday, perform the resection on a Thursday and send them back to the Sanatorium by ambulance on the fifth post-operative day. This has been done without harm to the patients. The large backlog of suitable patients who must be handled on limited funds has dictated this procedure. By and large, we are inclined to operate upon these patients and to resect the local lesions for smaller indications than in the more cooperative white patients. We operate them sooner after the institution of chemotherapy and (to get them while they are crying) before they have gotten to feeling so well that they want to disappear for parts unknown and discontinue their treatment.

The results have been encouraging, the mortality has been low, their confidence in and cooperation with sanatorium treatment, and in particular, their acceptance of surgery, their confidence in it and those caring for them have increased immeasurably over the years and the results likewise have improved. A complete report of these patients will be made at a subsequent date.

*IV. Tuberculosis in Children:*

Many children with primary tuberculosis even of rather extensive degree have, over the years, done exceptionally well with their primary process. Since the institution of chemotherapy, the prognosis has become considerably more favorable. Not all of them, however, are so fortunate. Some are cursed with extensive disease, some, in spite of chemotherapy or its late application, go on to destructive disease with cavitation, caseous abscesses, obstructive lobes with bronchiectasis or suppurating mediastinal nodes draining through the lung parenchyma. Such lesions have been seen occasionaly in white children but more commonly amongst the Indians. It is our feeling that the residual caseous lesions in these children are, if possible, considerably more dangerous than in adults.

It has been our practice for a considerable number of years to resect these lesions in the later teen-age group. More recently when confronted with similar conditions in younger children with lesions which have not responded completely to chemotherapy, we have resected as we would in adults without waiting for the patient to develop secondary troubles. We

have now performed seven partial lobectomies, 16 lobectomies and two pneumonectomies on 24 children under the age of 16 without mortality or complications. We have been gratified with the results obtained.

We have carried out total left pneumonectomy on a three and one-half year old Indian boy for a marked tuberculosis involving the entire left lung with large cavities in upper and lower lobes and considerable contralateral spread of disease in spite of intensive chemotherapy with a satisfactory result, clearing of the contralateral disease and the child remaining in good condition some five years after resection. The operations have been done only when other methods have failed and the patients have been left with residuals which we know from experience have been trouble-makers in the past.

*V. Mortality:*

The total mortality following resection at the Glen Lake Sanatorium for the years 1928 through 1955 covering 817 operations has been 1.95 per cent. This includes pneumonectomies, lobectomies, partial resections and bilateral resections in patients of all ages from 14 to 65 and includes the very early part of the series before the era of antibiotics, physician-anesthetists and all of the modern facilities. The early part of this series was the sole work of the author and that since 1950, the work of the three attending surgeons, Dr. Schmidt, Dr. Jensen and myself. There was no mortality in 1954 with 146 operations on 136 patients. There was one death in 165 operations on 149 patients or 0.6 per cent in 1955, and the total mortality for the two years, 1954 and 1955, 311 operations on 285 patients was one death or 0.3 per cent.

In my private service at St. Mary's Hospital from 1937 through April, 1956, we have carried out a total of 421 operations on 395 patients, 26 of them being bilateral resections, including 82 pneumonectomies with seven deaths, 192 lobectomies with seven deaths and 147 partial resections with no deaths; a total mortality of 3.64 per cent for lobectomy, 8.53 per cent for pneumonectomy. One must realize in considering these figures that a considerable number of these patients were in the salvage group previously mentioned, that not a few of them had been refused surgery elsewhere and a number had a total vital capacity of 1,000 cc. or less. Eight of these 14 deaths occurred amongst the 67 patients operated upon prior to 1951 before even short term chemotherapy against tuberculosis was effectively in the picture. The mortality for the 354 operations since 1950 was eight deaths

| | Glen Lake 1954-1955 311 Oper. Per Cent | St Mary's 1937-1956 421 Oper. Per Cent | St. Mary's 1951-1956 354 Oper. Per Cent |
|---|---|---|---|
| Pneumonectomy | 4.5 | 19 | 11 |
| Lobectomy | 20.58 | 45 | 48 |
| Partial Lobectomy | 74.92 | 34 | 41 |

or 1.7 per cent, all from lobectomy. A comparison of the various types of surgery between the Glen Lake and St. Mary's series is of interest.

The St. Mary's series carries a much higher percentage of the more serious resections. These figures compare favorably with the mortality figures from collapse therapy and most certainly resection is a more definite procedure than any type of collapse.

*VI. Complications:*

Prior to the institution of antimicrobial therapy of any type, complications were numerous and resection for tuberculosis was a hazardous procedure even under the most favorable circumstances. With drugs and antibiotics against secondary organisms, the number of complications was reduced but those from tuberculosis persisted. With the advent of adequate chemotherapy against tuberculosis, the incidence of complications dropped. Even with the short term chemotherapy of the early days, conditions became more favorable and even more so with more prolonged pre-operative and post-operative chemotherapy. The complications of resectional therapy in our modern era of intensive antimicrobial therapy against tuberculosis as well as secondary organisms are primarily related to resistance of the organisms, failure to completely obliterate space following resection, to primary air leakage, to hemorrhage and transfusion reaction, and to a miscellaneous small group of other causes.

Patients whose organisms have become resistant to drugs present a distinct hazard so far as serious complications and spread of disease are concerned. It was the hope that some of the newer short term drugs would help this situation but this has not always been so. This very fact presents additional argument against the indiscriminate use of the drugs and in favor of a well conceived, carefully planned program of treatment including plans for resection at an earlier more favorable time before resistance has had a chance to develop. Let us hope that in the future we will see fewer patients in this resistant category.

Failure to promptly obliterate pleural space following resection presents favorable conditions for fluid accumulation and for secondary and tuberculous infection with subsequent perforation of the lung and bronchial fistula. Much of the solution with this problem lies in the hands of the operating surgeon whose judgment and experience should dictate when the remaining lung will not adequately fill the space and when he should do a tailoring thoracoplasty at the time of his primary resection to bring this about. Many troubles may thereby be avoided. Residual pockets from parenchymal air leak or subsequent bronchial leak must be recognized promptly and adequate drainage of the pocket and obliteration of the space or closure of the fistula carried out promptly. Post-operative oozing with hematoma formation must be recognized early, the clots evacuated and the lung expanded to the chest wall without delay. That there are some complications to resections must be freely admitted. The complication rate at Glen Lake including the major and minor types, even the most trivial, for the years 1954 and 1955 was 15.4 per cent. The following complications (48) occurred following the 311 resections during these years:

| | |
|---|---|
| Pneumothorax | 15 |
| Hematoma | 10 |
| Empyema and Wound Infection | 6 |
| Bronchial Fistula | 4 |
| Shock | 3 |
| Pulmonary Embolism | 2 |
| Pneumonia | 4 |
| Miscellaneous | 4 |
| TOTAL | 48 |

The alertness of the whole therapeutic team in recognizing any complication early and treating it promptly has greatly reduced the incidence of serious complications. Time and experience have enabled the surgeon to avoid many of the pitfalls into which he has previously fallen.

### *Results*

The results from resectional therapy for tuberculosis are difficult to assess at this time. On the surface, they are excellent. A single procedure, of low risk, with few complications yet conservative and definitive in purpose has much to recommend it. By removing the essential remaining disease it offers a much shorter post-operative period of treatment and theoretically at least a safer future than from any type of collapse. The time is yet too short for a fair evaluation and the results are as yet clouded by the effects of long term chemotherapy still being continued. The number of resection patients who have had to be readmitted to the Sanatorium because of late reactivation of disease has been small over the years and most have occurred in those presenting organisms resistant to the drugs, those who early in the program received only short term therapy and the deserters who have disappeared and discontinued all treatment soon after surgery. Personally, as one who for the past 30 years who has utilized almost every type of surgical attack on this disease, I now feel that our present program is the best yet and that given modern facilities for its use, it is far superior to any other plan of attack now available.

## SUMMARY

Chemotherapy followed by resection of significant residual tuberculous disease has largely supplanted the prolonged bed rest and collapsed therapy program of a few years ago. The risk of resection (0.3 per cent in a total of 311 operations on 285 patients from 1954 to 1955) now is as low or lower than that by collapse therapy. Total mortality (60 days) for 817 operations at Glen Lake Sanatorium from 1928 through 1955 was 1.95 per cent. In special groups: (1) 25 resections in children under 14, no mortality; (2) In diabetics—3 pneumonectomies, 16 lobectomies, and 31 partial lobectomies on 40 patients, one death—mortality 2 per cent; (3) In Indians—175 operations on 164 patients—22 pneumonectomies, 52 lobectomies, 102 partial lobectomies, mortality rate 1.71 per cent. Complications

of all types, many not serious—15.4 per cent. Relapses or recurrences following chemotherapy and resection are closely related to short term chemotherapy and presence of resistant organisms and to incomplete treatment programs.


## RESUMEN

La quimioterapia seguida de la resección de las lesiones residuales de alguna importancia, ha suplantado ampliamente al plan de hace pocos años que consistía en el reposo prolongado y la colapsoterapia.

El riesgo de la resección (0.3 por ciento en un total de 311 operaciones en 285 enfermos de 1954 a 1955) es tan bajo o más bajo que en el colapso. La mortalidad total (60 días) para 817 operaciones en el Sanatorio Glen Lake desde 1928 hasta 1955 fué de 1.95 por ciento.

En grupos especiales: (1) 25 resecciones en niños menores de 14 años sin mortalidad; (2) en diabéticos 3 neumonectomías, 16 lobectomías, y 31 lobectomías parciales en 40 enfermos: una muerte-mortalidad 2 por ciento; (3) en indios—175 operaciones en 164 enfermos—22 neumonectomías, 52 lobectomías, 102 lobectomías parciales, mortalidad 1.71 por ciento.

Complicaciones de todas clases, muchas no serias 15.4 por ciento.

Recaídas o reactivaciones después de quimioterapia y resección, están íntimamente ligadas a la quimioterapia por corto tiempo y al la presencia de organismos resistentes así como a planes incompletos de tratamiento.



## ZUSAMMENFASSUNG

Die Chemo-Therapie mit nachfolgender Resektion bei in nennenswertem Umfang restierender tuberkulöser Erkrankung hat in weitem Umfang das Programm der langen Bettruhe und Kollaps-Therapie von vor wenigen Jahren ersetzt. Das Risiko der Resektion, nämlich 0,3% unter insgesamt 311 Operationen bei 285 Patienten zwischen 1954 und 1955, liegt jetzt ebenso niedrig oder noch niedriger als das bei Kollaps-Therapie. Die Gesamt-Mortalität (innerhalb von 60 Tagen) bei 817 Operationen im Glen Lake Sanatorium betrug ab 1928 bis Ende 1955 1,95%. Bei den einzelnen Gruppen lauten die Werte wie folgt: (1) 25 Resektionen bei Kindern unter 14 Jahren keine Sterblichkeit; (2) bei Diabetikern 3 Pneumonektomien, 16 Lobektomien und 31 partielle Lobektomien bei 40 Patienten 1 Todesfall d.h. eine Mortalität von 2%; (3) bei Indianern—175 Operationen bei 164 Patienten—22 Pneumonektomien, 52 Lobektomien, 102 partiellen Lobektomien, Sterblichkeitsziffer 1,71%. Komplikationen bei allen Operationsarten, vielfach nicht ernsthafter Natur, traten in 15,4% auf. Rückfälle oder frische Schübe nach Chemo-Therapie und Resektion stehen in engem Zusammenhang mit kurtzzeitiger Chemo-Therapie und dem Vorhandensein von resistenten Keimen und unvollständigen Behandlungsplänen.

# Rare Anomaly of the Aortic Arch Combined With Coarctation of the Aorta

A. N. ROMANOS, M.D., C. L. BRUINS, M.D. and A. G. BROM, M.D.
Leiden, Netherlands

## *Introduction*

Several reports on anomalies of the aortic arch concomitant with coarctation of the aorta are to be found in the literature.[3, 5, 7]

This paper describes such anomalies as they were found in two of our surgical cases, which showed unusual features not hitherto described in the literature available to us. These anomalies, although rare, are of practical importance with a view to differential diagnosis.

The etiology of coarctation is still obscure. The two cases presented in this paper should be taken into account in any attempt to explain the condition on the basis of embryological considerations.

The descriptions so far given in the literature stated that the right subclavian artery or the right aortic arch occurred distal to the coarctation.[1, 2, 8] We were unable to find a single report on a right subclavian artery or a double arch proximal to the coarctation. And it was precisely this condition which we found in the two patients to be described.

Edwards[4] recently described a case of Taussig-Bing complex with coarctation, in which the right subclavian artery arose proximal to the coarctation.

In the first of our two cases the right subclavian artery arose from the aorta above the coarctation; in the second case the double aortic arch was localized above the coarctation. In both cases the coarctation was found opposite the insertion of the ligamentum arteriosum.

*Case 1:** ** M. V., female, aged 19. The onset of symptoms, in 1946, was characterized by pain in the chest, loss of weight and fatigability, which continued until a severe hemoptysis occurred in 1948. Investigation at the time failed to reveal any tuberculous process but a mediastinal tumor was demonstrable by X-rays. The patient was referred to us at the St. Antonius Ziekenhuis, Utrecht.

The patient gave no impression of being very ill. The blood pressure determined in the arms was 150/90. Heart: slight systolic murmur. Pirquet tuberculin test: negative. Hematology normal. Fluoroscopy showed a tumor dorsal to the left main bronchus. The esophagus was displaced to the right. Tomography of the hilar region showed marked stenosis of the left main bronchus caused by the tumor. The presence of severe stenosis was confirmed by bronchography. Bronchoscopic examination showed that the bronchial wall was normal and that the stenotic part was still patent.

Angiocardiography: apparently satisfactory filling of the tumor with contrast medium suggested a probable aneurysm or a highly vascular neoplasm. Another severe hemoptysis occurred during the patient's stay in the hospital, this time causing what was considered vital danger. The blood pressure of 150/90 did not strike us as hypertension, and the possibility of coarctation was consequently not considered. An operation was performed in spite of an uncertain diagnosis.

The thorax was opened (March 3, 1949; surgeon: A. G. B.), and numerous adhesions were separated without difficulty. The first striking feature was found in the fact that a right subclavian artery arose distal to the left subclavian artery. The right radial pulse was suppressed when this vessel was clamped. The artery extended

*Academisch Ziekenhuis, Leiden, and St. Antonius Ziekenhuis, Utrecht.

**This case included in the thesis of A. G. Brom; "De Coarctatio aortae en haar behandeling."

to the right, behind the esophagus. About 1.5 cm. distal to the division into the right subclavian artery a multicolored tumor the size of an orange was found to arise from the aorta, which it completely surrounded over a length of almost 6 cm. with the exception of the left side of the aorta; this side was free but showed a slight depression in the aortic wall. This tumor was an aneurysm of the descending aorta arising immediately distal to a constriction of the aortic lumen at the level of the insertion of the ligamentum arteriosum (Fig. 1, a, c). The lumen of the aortic arch was slightly wider than that of the subclavian arteries, both of which were of small caliber. The caliber of the descending aorta distal to the aneurysm exceeded that of the arch and that of the descending aorta proximal to the aneurysm. The latter part showed a ventral adhesion with the lung to the right of the median line and a dorsomedial adhesion with the esophagus. The aneurysm was separated from the lung. At this point a hemorrhage from the aneurysm occurred, which was controlled with a finger. Dissection of the aorta was then attempted. This dissection and the subsequent ligation of the intercostal vessels were accomplished by routine procedure, in the course of which part of the membranous portion of the left main bronchus was resected with the aneurysm. The defect was closed with a free pleural graft.

The presumption that the aneurysm was the cause of the stenosis of the main bronchus and of the hemoptysis was confirmed. The minimal length of aorta to be removed in view of the stenosis and the aneurysm left a defect of 6 cm. End-to-end suture of the aorta was impossible. Since no aortic graft was available at the time (1949) the anomalous right subclavian artery was used to bridge the defect; an end-to-end anastomosis with the distal part of the aorta was made. This anastomosis provided a newly made aorta of lesser caliber than the arch but with a circumference exceeding 4 cm. (Fig. 1, b).

The operation was completed by routine procedure.

## *Pathology*

*Macroscopy:* The specimen had the size of an orange and consisted chiefly of a blood clot. A transverse section showed intermittent, probably aneurysmal dilations in the structure of the vascular wall. The vascular wall

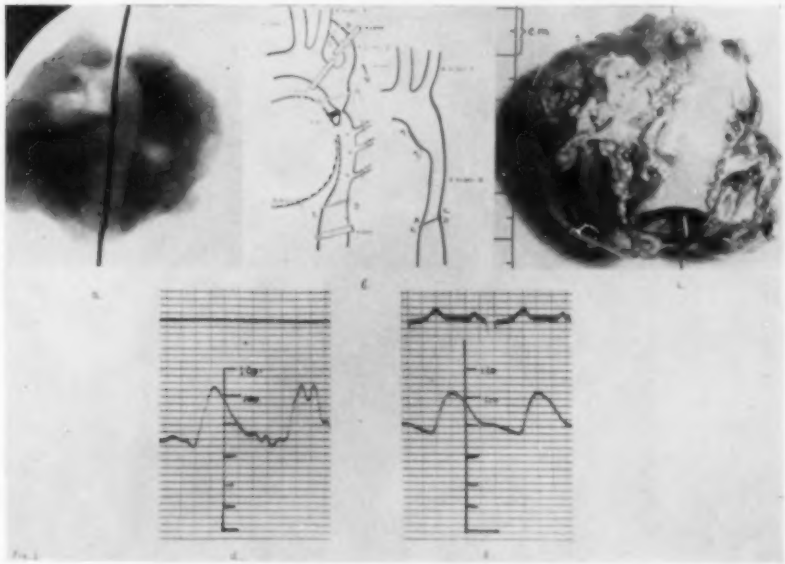

FIGURE 1: (a) X-ray of the specimen with the probe *in situ* in the aorta, (b) surgical findings and condition following resection (klem-clamp), (c) photography of specimen and (d and e) pressure readings in arms and legs, respectively, five years after the operation.

seemed to be of the usual thickness but the wall of the aneurysm was thinner.

*Microscopy:* the internal layer of the wall of the aneurysm was completely hyaline, with split formations, and with an inner lining of fibrin. The external layer showed a lamellar arrangement of hyaline fibres, with several diffusely spread round cells. No muscular tissue was found, and elastic tissue was only found in small scattered quantities. The irregular, broad adventitia contained a larger quantity of elastic tissue. A transverse section of the aorta showed marked intermittent thickening of the intima caused by degenerative changes (split formations, lipid deposits, hyalinization, necrosis and mucoid changes). Some degree of round-cell infiltration was seen in the irregular adventitia. The media was broad, causing the basic constriction of the lumen, and remarkably thick elastic bundles were found in between, with occasional patches of hyaline fibrous and muscle tissue. There was a marked diminution of fibrous elements in favour of elastic structures.

The postoperative course was uneventful. No pulse was palpable in the right arm. The patient was discharged three weeks after the operation and several periodic follow-ups were subsequently made.

FIGURE 2: X-ray of R. H. Marked left-sided enlargement of the heart. Esophagus showing impression of retro-esophageal vessel.

The last follow-up was made in March, 1954, i.e., five years after the operation, when the patient was referred to us by her obstetrician. She was pregnant and complained of headaches and dizziness. Nothing anomalous was found at examination. The pulsation of the femoral arteries synchronized with that of the left radial artery. The right radial artery was palpable but the amplitude was inconsiderable. Intra-arterial determination yielded blood pressure values of 120/80 in the left arm and 110/80 in the legs (Fig. 1, d, e).

*Case 2:* R. H., female, aged 2, of normal weight and with a deep, square thorax, slight scoliosis and atrophy of the limbs.

At the age of 21 months there was a period of left heart failure with unrest and marked orthopnea. Coarctation with pre- and post-stenotic hypertension was diagnosed. The blood pressure reading was 200/130 in the arms and 150/110 in the legs. Pulsation of collateral arteries was felt in both axillary regions. The ECG showed a sinus tachycardia of 144 with left axis deviation and left ventricular preponderance. Fluoroscopy revealed marked cardiomegaly, with presumable predominance of left-sided configuration; there was no evidence of pulmonary congestion. Contrast radiography of the esophagus did not indicate post-stenotic dilation of the aorta. The investigator at the time overlooked the constant impression of a retro-esophageal vessel extending in right superolateral direction such as is seen in cases of anomalous right subclavian artery or double aortic arch (Fig. 2). During angiocardiography the circulation was relatively slow, with satisfactory contrast in the right and left heart. The left auricle and ventricle were enlarged but the ascending aorta was not; there was circumscribed stenosis of normal localization. No post-stenotic dilation was observed.

Since there was no unmistakable evidence of left heart failure, no pre-operative digitalization was given.

During the operation (September, 1955; surgeon: A. G. B.) the patient had 16 attacks of cardiac failure with brief disappearances of blood pressure. Heart massage

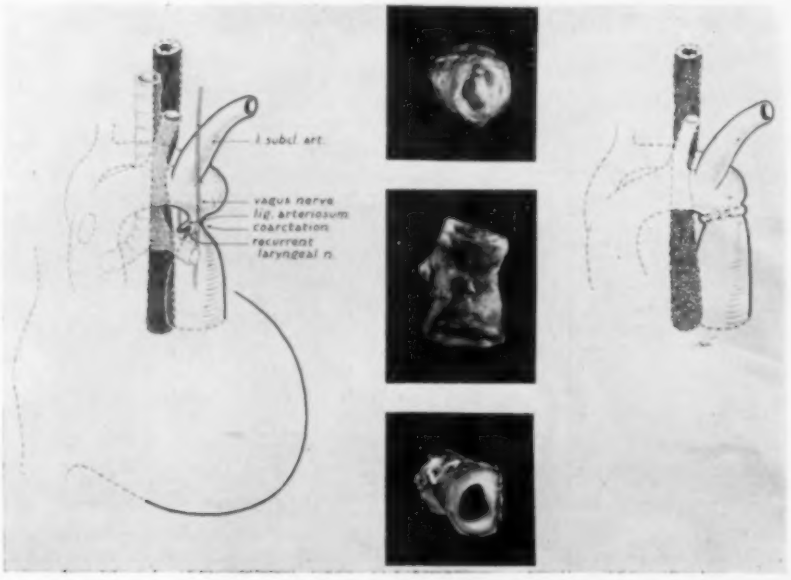


FIGURE 3: (a and c) Preoperative and postoperative findings and (b) photograph of the resected specimen.

was required during these periods. Surgical procedure was considerably impeded by this necessity, which made it almost impossible to secure a free field for dissection. In the course of dissection it was established that, immediately beyond the left subclavian artery, a second and equally large vessel arose from the aortic arch, extending to the right behind the esophagus. There was no cessation of the right pulse when this vessel was clamped off. A double aortic arch was therefore presumed to exist. The coaretation was localized at the site of junction of the ligamentum arteriosum. Dissection of the coarctation required considerable effort (due partly to the degree of weakness of the heart). Pott's clamps were placed on the aorta. The stenotic part was resected and an end-to-end anastomosis was made, using interrupted sutures (Fig. 3). The anastomosis obtained after removal of the clamps was certainly as large as the arch. Cardiac arrest recurred after closure of the thorax, which was then re-opened for heart massage. The blood pressure subsequently returned.

The attacks of cardiac failure may have been due either to hypersensitivity of the left hilus to manipulation or to mild pulmonary edema (the lung felt somewhat spongy).

The ECG recording during cardiac failure showed (Fig. 4) slowing of the sinus rhythm with occasional ventricular arrest (skipped beat). The deceleration in rhythm was followed by an increase in frequency associated with merging of the P-top with the preceding T-top. These findings seemed to suggest that, even during maximal tachycardia, the underlying rhythm originated in the sinus node in the normal manner.

In the course of the operation there was an alarmingly progressive widening of the QRS-segment with a marked depression in the ST-wave. Yet even at this stage the arterial pressure was fairly constant at 160/85 (and at 140/85 after elimination of the coarctation).

During the operation there was a steady rise in the temperature, which reached 41° C. at the end. The patient was cooled in an ice bath after the operation. She was removed from the bath at 36.7° C., but cooling continued. The ECG still showed marked widening

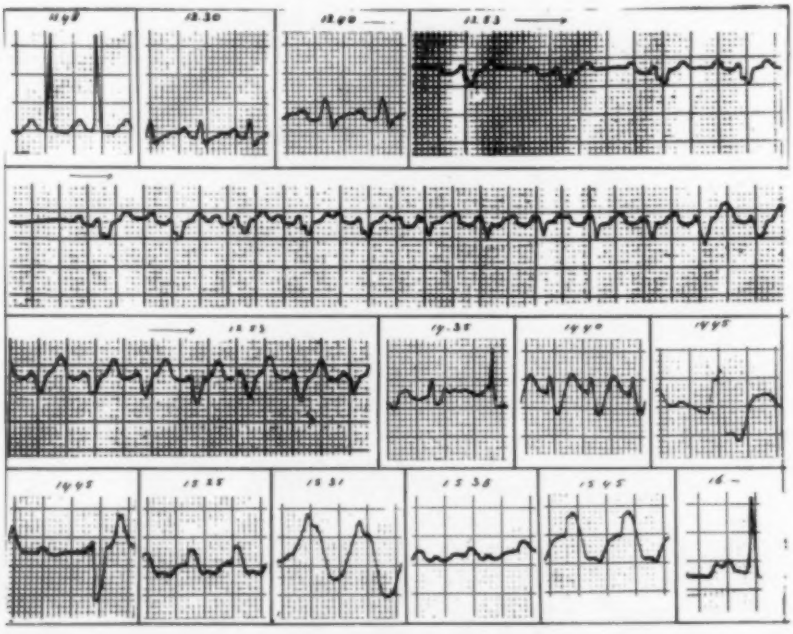

FIGURE 4: Standard limb lead I; time: 11:48 induction of anesthesia; normal rhythm. 12.30-12.40 open thorax; sinus rhythm. 12.53 clinical cardiac arrest followed by sinus rhythm with increased frequency and widening of QRS-segment. 14.35 extrasystole. 14.45 during and after cardiac arrest. 15.25 in ice bath. 16.00 after acute return to normal. Throughout the procedure there was a progressive widening of the QRS-segment with a marked depression in the ST-wave.

of the QRS segment; this did not respond to cedilanid but showed a spontaneous, acute return to normal at a temperature of 34° C. (Fig. 5).

Two weeks after the operation the child was discharged in good condition. The double aortic arch was not ligated, as the patient's general condition during the operation did not allow of any but the absolutely unavoidable manipulation, and as preoperative examination revealed nothing to suggest that this condition impeded swallowing or respiration.

Two months after the operation the patient was in good general condition when seen at follow-up. The size of the heart showed a decrease. Determination of blood pressure by arterial puncture yielded the following values:

| | |
|---|---|
| RA 145/75 | RL ..... |
| LA 160/90 | LL 150/75 |

## *Discussion*

A series of 172 cases of coarctation given surgical treatment since 1948 included the two above described cases of a rare anomaly of the aortic arch concomitant with coarctation of the aorta.

The first patient presented an anomalous right subclavian artery arising between the left subclavian artery and the coarctation. This vessel was undoubtedly the right subclavian artery, as shown by the fact that the pulse in the right arm disappeared as soon as the vessel was severed, whereas preoperative determinations revealed the same brachial pressure bilaterally. The pulse did not re-appear until three months after the operation; its amplitude was then inconsiderable. Follow-ups covering a period of more than five years showed, moreover, that the surgical results were in no way

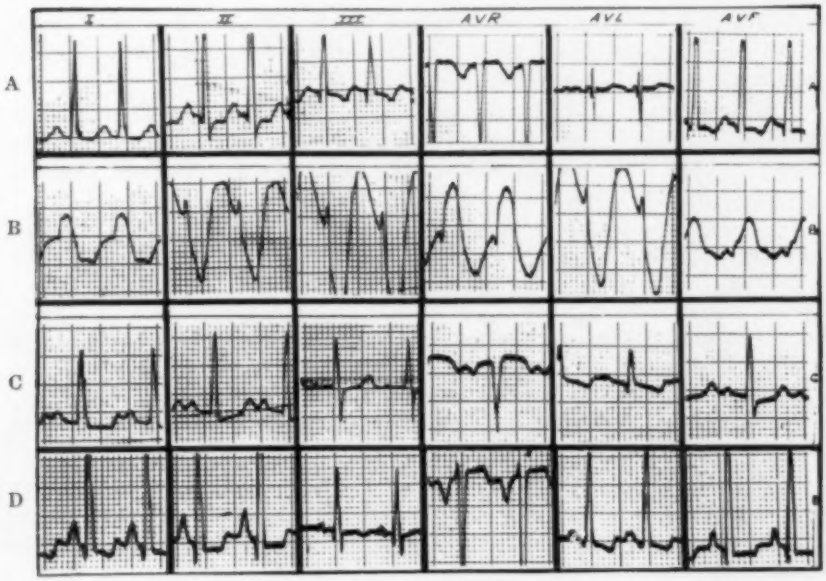


FIGURE 5: ECG limb leads a, b and c during anesthesia (a) before thoracotomy (b) after closure of the thorax and immersion in ice water, temperature about 36° C., (c) ten minutes after b, temperature about 34° C. (d) Return to normal rhythm.

impaired by the fact that the anastomosis made was smaller in caliber than the proximal part of the aorta. The patient's blood pressure was on the low side rather than high, even during pregnancy. We disagree with Gross[6] as to his claim that the anastomosis should have a lumen at least as large as that of the aortic arch.

Optimal results in adults are ensured if the circumference of the anastomosis is 4 cm. or more. We believe also that the shape of the arch following anastomosis is of importance and should approximate the normal anatomical aspect as closely as possible.

In the second case a wide, patent right aortic arch was found proximal to the coarctation. Both arches were nearly equal in caliber, the right being slightly less wide than the left. Pre- and postoperative determinations revealed almost the same pressure in both arms. The pulse in the right arm remained unaltered throughout the operation, even when both arches were clamped. The preoperative esophageal findings were such as to suggest an aortic ring although there were no symptoms of dysphagia lusoria. The complete absence of tracheal compression and the unusual technical difficulties encountered prevented severance of the right arch.

It should be emphasized that a characteristic picture of coarctation of the aorta was found in both cases.

## SUMMARY

Two cases of rare anomalies of the aortic arch combined with coarctation of the aorta are described.

In the first case the anomalous right subclavian artery arose proximal to the coarctation and was successfully used to bridge the defect resulting from resection of the coarctation.

The second case presented a patent right aortic arch, likewise proximal to the coarctation. Intervention in this case had to be limited to the coarctation in view of the absence of tracheal compression and the technical difficulties encountered.

In both cases the aortic stricture presented the characteristic features of coarctation of the aorta.

## RESUMEN

Se relatan dos casos de anomalías raras del arco aórtico combinadas con coartación del istmo.

En el primer caso la arteria subclavia anómala salía arriba de coartación y fué usada con éxito como un puente sobre el defecto después de la resecién de la coartación.

En el segundo caso arco aórtico derecho abierto se encontró otra vez arriba de la coartación. En este, tratamos sólo la coartación ya que no había compressión de esófago y también por las dificultades técnicas durante la operación.

En ambos casos el estrechamiento aórtico tenía las características de la estenosis ístmica de la aorta.

## RESUME

Les auteurs rapportent deux cas d'anomalies rares de l'arc aortique associées à un rétrécissement de l'isthme.

Dans le premier cas une artère sous-clavière droite anormale prenait naissance au-dessus de la coarctation et put être utilisée avec succès pour rétablir une situation normale après résection de la coarctation.

Dans le second cas, un arc aortique droit évident fut constaté au-dessus de la coarctation. Dans ce cas, les auteurs ne se sont occupés que de traiter la coarctation, étant donné l'absence de compression oesophagienne, et les difficultés techniques apparues lors de l'intervention.

Dans les deux cas, le rétrécissement aortique présentait le tableau caractéristique des sténoses isthmiques de l'aorte.

## ZUSAMMENFASSUNG

Bericht über 2 Fälle seltener Anomalien des Aortenbogens in Verbindung mit Verengung des Isthmus.

Bei dem ersten Fall entsprang die abnormale rechte Arteria subclavia oberhalb der Verengung und diente mit Erfolg zur Überbrückung des Defektes nach Resektion der Verengung.

Bei dem 2. Fall wurde wieder oberhalb der Verengung ein offener rechter Aortenbogen gefunden. In diesem Fall befassten wir uns nur mit der Verengung wegen des Fehlens einer Speiseröhren-Kompression und der technischen Schwierigkeiten währnd des Vorgehens.

In beiden Fällen wies die Aortenstriktur das charakteristische Bild einer Isthmus-Stenose der Aorta auf.


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# A Technique of Bronchography with Visciodol: A New Contrast Medium

ERGI J. PESIRI, M.D. and WALDRON M. SENNOTT, M.D.*
Staten Island, New York

Since the first bronchography was performed by Chevalier Jackson[1] in 1918 with the use of bismuth powder insufflated through a bronchoscope, there has been a constant search for more satisfactory bronchographic contrast media. The procedure did not gain widespread acceptance until the epoch making discovery by Sicard and Forestier[2] in 1923, that Lipiodol made a satisfactory contrast medium for this examination. Other iodized oils were subsequently introduced, but none was able to surmount the following common objections to their use for this procedure:

1) Retention within the alveoli obscures any accurate follow-up for long periods of time, as elimination from the lung is slow.

2) The retained iodine interferes with any subsequent radiation therapy.[3]

3) Delay in any contemplated pulmonary surgery due to an increased incidence of post-operative atelectasis in cases having had recent bronchography with alveolar penetration.[4]

4) Alveolograms are far more difficult to interpret than bronchograms.

5) Reported formation of iodized oil granulomas.[5]

6) Prolongation of reactions in iodine sensitive individuals due to slow liberation of iodine.

7) Repeat bronchograms impossible for long periods of time due to obscuring shadows of alveolar oil.

These objections led to the introduction of water-soluble contrast agents. Ioduron B and Umbradil Viscous B were introduced in 1948. More recently Dionosil Aqueous in a carboxymethylcellulose base has become available. These agents are not without their own particular group of inherent objectionable qualities. We feel, as do other workers,[6, 7] that these objectionable qualities makes their use as undesirable as the use of the unaltered iodized oils for this procedure. The chief objections to the use of these water-soluble agents are:

1) They produce severe local irritation and require deep topical anesthesia.[6, 7]

2) The radiographic images produced by these agents are less dense than those produced by the iodized oils due to lower iodine content. This is particularly important on the lateral projection.[8]

3) Undue haste must be employed during the procedure due to their rapid absorption.

4) The carboxymethylcellulose present as the base of these agents has

*United States Public Health Service Hospital.

been shown to produce an inflammatory response which may be severe and irreversible.

5) Large quantities of these agents are required to produce adequate filling of the bronchial tree, usually 20 or more cc. per lung.[9]

6) The miscibility of the carboxymethylcellulose with the bronchial secretions may produce secretions so viscid that a respiratory emergency ensues. An emergency bronchoscopy with bronchial suction may be necessary as a life saving procedure.[10]

Recently, Dionosil in an oily base has become available. This preparation is an improvement over the water-soluble agents, however, it too has some inherent objectionable qualities. The most common objections to the use of this agent are:

1) Greater tendency to alveolar penetration than the water-soluble agents.[11]

2) A large amount of this agent must be used in order to obtain a satisfactory outline of the bronchial tree, usually 20 cc. per lung.

3) In spite of its arachis oil base, this preparation is still more irritating that the iodized oils, requiring deeper anesthesia.[12]

4) The iodine content of this agent is 34 per cent, the iodine content of Lipiodol is 40.

5) The fate of the radiolucent arachis oil base has never been completely studied. Some of the oil undoubtedly remains in the lung, although not visible on the radiograph, and could possibly give rise to any of the known complications due to oil in the lung. However, to date, no such complications have been reported.

6) There is a tendency for Dionosil Oily to drain from the upper lobe bronchi during the procedure.

### *Material*

During the past nine months, the authors have had the opportunity to perform 35 bronchographies with Visciodol, a Lipiodol-sulfanilamide suspension (E. Fougera & Co., Inc.). The formula of this preparation as given by the manufacturer is:

| | |
|---|---|
| Sulfanilamide | 0.32 gm. |
| Sodium sulfite | 0.002 gm. |
| Lipiodol, 40 per cent q.s. to | 1 cc. |

The finely divided sulfanilamide is added as an inert agent in order to increase the viscosity of the Lipiodol, thereby practically eliminating alveolar penetration. The bland properties of Lipiodol are retained and all the problems associated with alveolization are eliminated. The small amount of sodium sulfite is added to prevent any liberation of free iodine on contact with air thus insuring a non-ionic iodine complex.

### *Premedication*

Our routine pre-bronchographic orders have been:

1) No lunch.

2) Demerol 50 mg. at 1:00 P.M.

3) Nembutal 100 mg. at 1:00 P.M.

4) Atropine 0.4 mg. at 1:00 P.M.

5) To the Radiology Department at 2:00 P.M.

Following the procedure, we have not permitted eating or drinking for three hours in order to prevent possible aspiration.

*Technique*

All bronchographies in this series were carried out with the use of Xylocaine topical anesthesia. The rapidity of action and great potency of this agent makes it particularly suitable for use in conjunction with this procedure. A minimum of anesthetic agent is required in order to obtain a satisfactory degree of anesthesia.

This series was carried out using the catheter intubation method. In all but one case the catheter was inserted by using the Haight maneuver.[12] Our routine consists of coating the sides of the distal portion of the catheter with a small amount of xylocaine jelly. The catheter is inserted into the larger of the two nares. When the patient no longer has any discomfort due to the presence of the catheter, the head is tilted slightly forward, the tongue pulled forward, and the catheter advanced as far as the arytenoids. The presence of the catheter at this level stimulates the cough reflex. When this occurs the catheter is withdrawn slightly and is quickly advanced simultaneously with the expiratory phase of the cough or during the deep inspiration which follows. Should the patient tend to swallow the catheter, this can be avoided by withdrawing the catheter slightly, and advancing and withdrawing it in quick succession, stimulating the cough reflex. This method eliminates the necessity of anesthetizing the oropharynx, and also eliminates the use of the laryngeal mirror, and special instruments for inserting the catheter.

The one case in which the catheter could not be inserted using this

FIGURE 1: Bronchogram performed with 5 cc. of Visciodol for each lung, practically complete elimination in twenty-four hours, no alveolization.

method occurred in a patient with an unusually large tongue. A laryngeal mirror and anesthetization of the oropharynx was used in this patient.

Once the catheter enters the trachea a paroxysm of coughing is encountered. Immediately 8 to 10 cc. of a 2 per cent Xylocaine solution is injected through the catheter. Within less than a minute the cough response will be suppressed. Following this the patient is placed on the fluoroscopy table in the supine position and the remainder of the examination carried out under fluoroscopic control. The catheter is advanced into the desired main-stem bronchus by having the patient turn his head as far lateral away from the side desired. The catheter is then advanced and will usually enter the desired bronchus; occasionally this maneuver may have to be repeated one or more times. The catheter is then positioned to rest just above the orifice of the upper lobe bronchus. The side which is most suspected for pathology is examined first.

The Gianturco technique[13] with minor modifications is used for the actual outlining of the bronchial tree. The patient is placed in the lateral decubitus position, the side to be filled dependent. An additional 1 cc. of Xylocaine solution is injected through the catheter at this time in order to fully anesthetize the upper lobe bronchi. This step is of paramount importance in suppressing the cough reflex during the procedure. The patient is then instructed to breathe deeply and slowly and over the course of several respirations the medium is injected. Although the Visciodol is injected fairly rapidly, the patient does not experience any sensations of drowning. The amount of Visciodol used varies inversely with the patient's ability to breathe deeply—8-10 cc. is usually necessary. In one cooperative 19 year old patient (Fig. 1) we were able to achieve excellent

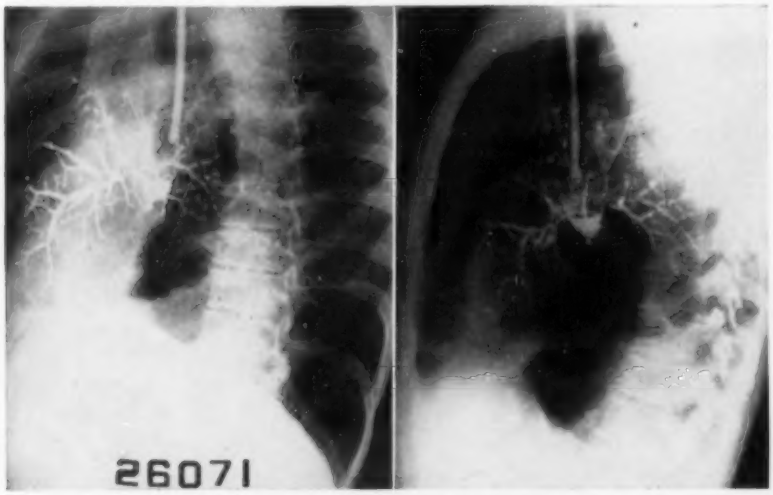


FIGURE 2: Post-operative examination, patient had previous lower lobectomy and lingulectomy. Note high density shadow produced on the lateral as well as the oblique projection.

coating of the entire bronchial tree with the use of 5 cc. for each lung.

We have found it necessary to turn the patient into the prone position and inject an additional 1 or 2 cc. to completely outline the middle lobe or lingula. After the examiner decides that filling appears adequate, spot films, as deemed necessary are made. The patient is then taken to the radiography room and six foot postero-anterior, lateral and posterior oblique projections are made. The films are checked in the wet state and the degree of filling assessed; if necessary, more contrast material can be injected at this time and further films made. We have found this necessary in only one case. The patient is then returned to the fluoroscopy room and the catheter is inserted into the opposite bronchus and positioned as previously described. The patient is then placed in the opposite decubitus position, 10 cc. of contrast medium is injected exactly as before except for the fact that it is done without fluoroscopic control. The filled bronchi of the opposite side cast too many interfering shadows on the fluoroscopic screen to make fluoroscopy in the lateral position of any real value. After this 10 cc. has been injected, the patient is obliqued slightly so as to separate the two bronchial trees and the filling checked with the fluoroscope. When it is decided that filling is satisfactory, the patient is taken to the radiography room and a routine postero-anterior or a stereo-postero-anterior projection as well as a posterior-oblique projection is made. Our findings confirm those of Dapra[14] that the high density of the shadow cast by the Visciodol makes stereo projections practical as well as informative. The posterior-oblique projection is preferred since it places the bronchi closer to the cassette, diminishing the magnification, and increasing the clarity of the image.

Every effort should be made to keep the exposure time under 1/10 of a second in order to avoid blurring of the basilar bronchi due to transmitted cardiac motion. In exceptionally large patients it may be necessary to

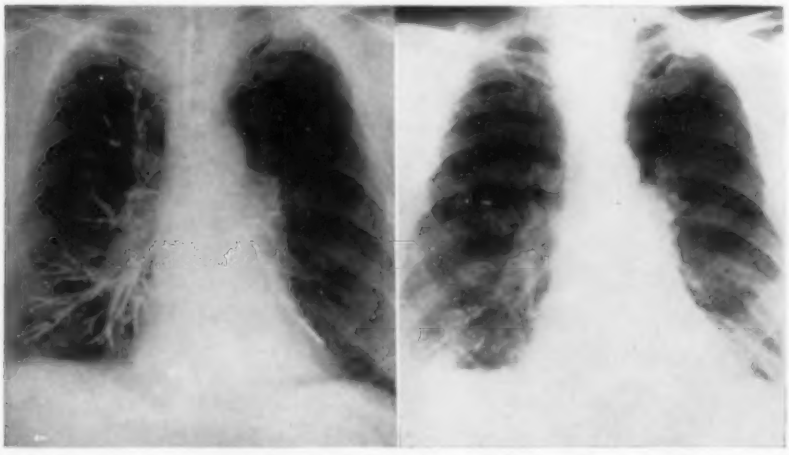

FIGURE 3: Minimal retention within the major bronchi, no evidence of alveolar penetration in a patient having minimal bronchiectatic changes in the right base.

reduce the tube-cassette distance to 40 inches to keep the exposure time within acceptable limits.

In every case the patient is instructed to cough vigorously as soon as the procedure is completed. Most of the Visciodol is eliminated at this time. Postural drainage has not been ordered as a routine follow-up. A 24 hour film is routinely made. At this time a small amount of Visciodol is usually present in the larger bronchi, and none in the alveoli (Fig. 3, 4). The small amount in the larger bronchi is expectorated within the next few days. In only one case did any significant degree of alveolization occur. In this case the medium had been heated prior to administration which may have been a factor in the alveolar penetration. It is recommended that the medium not be heated prior to administration as this lessens the viscosity.

### *Product*

As previously stated, this entire series was carried out with the use of Visciodol contrast medium. A Lipiodol-sulfanilamide suspension for bronchography was first used by Dormer and his associates[15] in 1945. These workers were interested in any possible therapeutic effect; however, they did note the excellent quality of the bronchograms obtained with this suspension. Houghton and his co-workers[3, 16] subsequently reported the use of up to 10 grams of sulfanilamide suspended in 20 cc. of Lipiodol without untoward results. These workers reported 7,000 bronchograms performed with Lipiodol-sulfanilamide suspensions. All reports in the literature,[3, 6, 14, 15, 16, 17, 18] predominantly European, have been favorable, stressing the minimal alveolization and rapid elimination from the lungs. We have been particularly impressed with the minute degree of alveolar penetration, the high density of the image produced, the lack of irritation

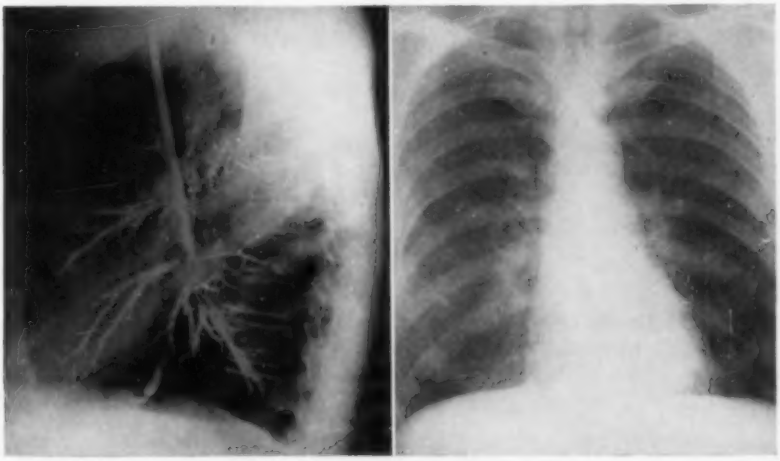

FIGURE 4: High density of the shadow produced on the lateral film, minimal retention within the major bronchi at 24 hours, no alveolar penetration. Esophagus outlined by swallowed medium.

and the rapid elimination of the medium. We feel, to date, that Visciodol is the agent of choice for bronchography.

### *Toxicity*

In one case previously known to be sensitive to sulfonamides, in whom we neglected to elicit this history, a transient sulfonamide reaction was encountered. This responded rapidly to anti-histamine medication. We now make an especial attempt to elicit any previous history of sensitivity. We have not administered prophylactic ACTH or anti-histamines prior to the procedure as has been recently reported.[18]

### *Discussion*

A full discussion of all the indications for bronchography is beyond the scope of this report, however, the following criteria are used as justification for performing the procedure by the authors:

1) Bronchiectasis suspected on the routine films with some associated clinical symptomatology.

2) Bronchiectasis suspected clinically regardless of the appearance of the routine films.

3) Pulmonary tuberculosis refractory to therapy, before or after thoracoplasty.

4) Evaluation of any cystic abnormalities of the pulmonary parenchyma.

5) Diagnosis of obstruction of the bronchi not accessible to the bronchoscope.

6) Any case of idiopathic hemoptysis where the source of bleeding is likely to be pulmonary. The value of having bronchiectatic areas mapped in advance, in such cases, is well substantiated.[19]

7) Any case of carcinoma of the lung where a knowledge of the status of the bronchial tree is desired prior to surgery.

8) Any case of suspected alveolar cell carcinoma, in an attempt to confirm the impression by demonstrating narrowing of the bronchial tree.[20]

With the use of the previously described techniques, the procedure becomes a rapid one (30 to 45 minutes), produces little patient discomfort, and yields a tremendous return in information gained. The use of Visciodol speeds the procedure, increases its safety by diminishing the amount of anesthesia necessary and provides higher quality radiographs.


## SUMMARY

1. The authors' experience with Visciodol, a Lipiodol-sulfanilamide suspension, for use in bronchography has been presented.

2. This agent enables one to obtain excellent bronchograms and practically never penetrates the alveoli.

3. We feel Visciodol is the contrast medium of choice for bronchography.

## RESUMEN

1. Se presenta el resultado de la experiencia de los autores usando el Visciodol, que es una suspensión de Lipiodol y sulfanilamida.

2. Este producto permite obtener excelentes broncogramas y prácticamente nunca penetra en los alveolos.

3. Creemos que el Visciodol es el medio de contraste de elección para la broncografía.

RESUME

1. Les auteurs présentent les résultats de leur expérience concernant l'utilisation pour la bronchographie du "Visciodol," suspension de lipiodol et de sulfamide.

2. Ce produit permet l'obtention d'excellentes bronchographies et pratiquement ne pénètre jamais dans les alvéoles.

3. Les auteurs pensent que le visciodol est le produit de contraste de choix pour la bronchographie.

ZUSAMMENFASSUNG

1. Es wurden die Erfahrungen der Verfasser mit Visciodol, einem Lipiodol-sulfanilamid-Suspension zum Gebrauch bei der Bronchographie vorgelegt.

2. Dieses Mittel ermöglicht es, ausgezeichnete Bronchogramme zu erhalten, und dringt praktisch niemals in die Alveolen ein.

3. Verfasser drücken die Überzeugung aus, dass Visciodol das Krontrastmittel der Wahl für die Bronchographie darstellt.

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# Plasma Glycoproteins in Pulmonary Tuberculosis*

DAVID SALKIN, M.D., F.C.C.P., S. H. LAWRENCE, M.D., and
HENRY E. WEIMER, Ph.D.

San Fernando, California

The glycoproteins of plasma are a heterogeneous group of conjugated proteins consisting of polysaccharides in firm union with peptides or proteins.[1] Increased interest has been shown in this group of proteins in the past few years due to the demonstration that their concentration is markedly increased in a number of pathologic and physiologic states.[2] With respect to infectious diseases, the carbohydrate-containing proteins of serum have been studied most extensively in relation to tuberculosis. Marked increases in the total serum glycoprotein have been reported in clinical tuberculosis[3-8] and in experimental tuberculosis of guinea pigs[9] and of rabbits.[10] Elevated levels of the seromucoid (mucoprotein) fraction have been observed in clinical tuberculosis[8] and in the experimental disease in guinea pigs.[9]

Recently, Method 10 developed by Cohn and associates[11] has been adapted by Lever and co-workers for the fractionation of 5 ml. amounts of human plasma into four primary fractions.[12] It seemed possible that such a method might provide more information on the response of the carbohydrate-containing proteins to pulmonary tuberculosis than could be obtained from total plasma glycoprotein and seromucoid determinations.

In the present investigation, 5 ml. of plasma samples from normal individuals and from patients with minimal, moderately advanced and far advanced tuberculosis have been separated by the low temperature-low salt-ethanol procedure of Lever[12] into four primary fractions, protein-bound carbohydrate (hexose) and protein have been measured in the fractions and the results have been correlated with total glycoprotein, seromucoid, and total protein determinations on whole plasma.

## *Materials and Methods*

*Plasma:* Seventeen ml. of blood were obtained by venipuncture. The blood was immediately added to 3 ml. of A.C.D. solution.[12] Following separation by centrifugation from the blood cells, the A.C.D. plasma was stored at minus 20° C. until the fractionations and the chemical determinations could be conducted.

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*From the Veterans Administration Hospital, San Fernando, California; and the Departments of Infectious Diseases and Medicine, School of Medicine, University of California, Los Angeles, California.

Technical assistance of Jean Redlich-Moshin.

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*Fractionation:* Five ml. aliquots of A.C.D. plasma were fractionated by the low temperature-low salt-ethanol procedure of Lever and associates into 4 primary fractions: I plus III, II, IV plus V, and VI. The separations were performed in a minus 5° C. bath containing 50 per cent by volume of ethanol and equipped with an effective stirrer. Precipitates were recovered by centrifugation at minus 5° C. in an International Refrigerated Centrifuge, Model PR-1, equipped with an angle head.

*Chemical Analyses:* Fractions I plus III, II and VI were dissolved and made up to 10 ml., and Fraction IV plus V was dissolved and made up to 25 ml. with the same reagents employed by Lever et al. The protein-bound carbohydrate (hexose) content of the plasma fractions was determined as follows: One ml. aliquots of the protein solutions were added drop-wise to 10 ml. absolute ethanol at room temperature. After standing 10 minutes, the precipitate was centrifuged at 1800 R.P.M. for 10 minutes. The ethanol was decanted and the precipitate drained by inverting the tube. One ml. of distilled water was added and the hexose content determined by an orcinol reaction.[9] The protein content of the isolated fractions was estimated in 1 ml. aliquots by the biuret method of Weichselbaum.[13] Albumin was determined in Fraction IV plus V by the hematin-binding procedure of Rosenfeld and Surgenor.[14] Total plasma glycoprotein, seromucoid, and total plasma protein were determined by methods previously reported.[9] The mean, standard error of the mean, *t*, and probability values were determined by standard statistical methods.[15]

## *Clinical Methods*

Determinations were carried out on a total of 56 patients. Three were eliminated in the National Tuberculosis Association classification because their disease consisted only of pleural effusion. For the clinical estimations only those patients were evaluated on whom complete clinical and x-ray film data were available.

In determining the significance of the proteins, glycoproteins, and seromucoid in clinical tuberculosis a number of factors were evaluated. They included other laboratory determinations such as blood counts and sedimentation rates; bacteriological studies of secretions for *M. tuberculosis* by smear, culture and guinea-pig; roentgen studies of a serial nature with the use of both regular and supplemental views; such clinical features as evidences of toxicity, fever, weight, and the course of the disease; such characteristics as age, sex, race; and the treatment of the patient including chemotherapy and surgery.

*Characteristics of the Patients:* All of the 56 patients were men with a mean age of 41 years and a range from 21 to 68 years. The racial distribution was 48 white, six Negro, and two oriental; of the white group seven were of Latin-American extraction.

At the time of the blood studies, all patients had active tuberculosis in some degree as determined by serial roentgen and bacteriological studies. A number of patients had shown considerable improvement and were even

TABLE I

DISTRIBUTION OF PLASMA GLYCOPROTEINS IN PULMONARY TUBERCULOSIS

| CLASSIFICATION | NORMAL | | MINIMAL | | | MODERATELY ADVANCED | | | FAR ADVANCED | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Number of Cases | 20 | | 7 | | | 20 | | | 26 | | |
| Component | Mean* (mg. per 100 ml.) | Per Cent of Total | Mean* (mg. per 100 ml.) | P | Per Cent of Total | Mean* (mg. per 100 ml.) | P | Per Cent of Total | Mean* (mg. per 100 ml.) | P | Per Cent of Total |
| TOTAL | 109 ± 2.1 | 100.0 | 109 ± 4.2 | 1.0 | 100.0 | 104 ± 2.7 | 0.1 | 100.0 | 143 ± 4.4 | 0.001 | 100.0 |
| Sum of Primary Fractions | 105 ± 2.0 | 96.3 | 103 ± 3.8 | | 94.5 | 98 ± 2.6 | | 94.2 | 139 ± 6.2 | | 97.2 |
| Fraction I + III | 38 ± 1.2 | 34.9 | 37 ± 2.4 | 0.5 | 33.9 | 33 ± 1.3 | 0.01 | 31.7 | 46 ±2.1 | 0.01 | 32.2 |
| Fraction II | 13 ± 0.7 | 11.9 | 13 ± 0.6 | 1.0 | 11.9 | 11 ± 0.6 | 0.01 | 10.6 | 16 ± 0.3 | 0.01 | 11.2 |
| Fraction IV + V | 41 ± 1.2 | 37.6 | 39 ± 2.7 | 0.2 | 35.8 | 40 ± 1.6 | 0.5 | 38.4 | 53 ± 2.3 | 0.001 | 37.0 |
| Fraction VI | 13 ± 0.5 | 11.9 | 14 ± 0.8 | 0.05 | 12.9 | 14 ± 0.8 | 0.2 | 13.5 | 24 ± 1.3 | 0.001 | 16.8 |
| Seromucoid | 10 ± 0.4 | 9.2 | 9 ± 0.8 | 0.05 | 8.3 | 10 ± 0.4 | 1.0 | 9.6 | 18 ± 1.4 | 0.001 | 12.6 |

*Including the Standard Error of the Mean.

classified as arrested but none showed truly healed and inactive disease The extent of disease was minimal in seven, moderate in 20, and far advanced in 26 patients. Cavitation was present in 23 of the far advanced group and in four of the moderate group.

All had specific chemotherapy with various combinations of streptomycin, isoniazid, and para-aminosalicylic acid; at the time of the blood studies all but seven were receiving the drugs. The surgical measures, at the time, included seven pneumoperitoneums, one thoracoplasty, and four pulmonary resections. Significant emphysema was present in seven and pleural fluid in three patients.

*Definitions:* The *extent of the disease* was determined in two ways, by the usual National Tuberculosis Association classification into minimal, moderately advanced, and far advanced groups[16] and by the percentage of both lungs involved by the tuberculous process. It is appreciated that the latter estimate is fraught with many difficulties and depends much on personal judgment; nevertheless it was felt that a fairly good approximation was made because of the comprehensive roentgen studies and the closeness of separate determinations by two of the authors.

The *pathological characteristics of the disease* were divided into the classical exudative, productive, and fibroid groups and their combinations. The exudative infiltrations were further subdivided as to the "degree of exudation" viz. one plus, two plus, and three plus to characterize respectively a mild, moderate, and high degree of exudation.

The *roentgen estimate of activity* was based upon the extent of the disease and the predominant pathological characteristics with special reference to the degree and extent of the exudative element and the size and character of the cavitation present. This grading was made on a 10-point scale for working purposes and then grouped into low,[1-2] moderate[3-5] and high[6-10] degrees of activity.

The *clinical estimate of activity* was based upon the roentgen estimate described above; the course of the disease to date, whether progressive, stationary, or regressive; such clinical features as toxicity, fever, and weight; and hematological and any other abnormalities. The grading was again made on a 10-point scale and then grouped into low,[1-3] moderate,[4, 5] and high[6-10] degrees of activity.

## *Results and Discussion*

*Normal Values:* The mean values per 100 ml. plasma was 7.4 gms. for total protein, 109 mg. for total glycoprotein, and 10 mg. for seromucoid. The upper limits of normal are hard to define but, in this paper, total glycoprotein values above 125 mg. and seromucoid above 14 mg. were considered abnormal.

The concentration of the *total glycoprotein* (Table I) was greatest in Fraction IV + V (alpha globulin plus albumin) followed closely by Fraction I + III and with equal amounts in the other two fractions. The chief component of Fraction VI and seromucoid is orosomucoid, a glycoprotein

TABLE II

DISTRIBUTION OF PLASMA PROTEIN IN PULMONARY TUBERCULOSIS

| CLASSIFICATION | NORMAL | | MINIMAL | | | MODERATELY ADVANCED | | | FAR ADVANCED | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Number of Cases | 20 | | 7 | | | 20 | | | 26 | | |
| Component | Mean* (gm. per 100 ml.) | Per Cent of Total | Mean* (gm. per 100 ml.) | P | Per Cent of Total | Mean* (gm. per 100 ml.) | P | Per Cent of Total | Mean* (gm. per 100 ml.) | P | Per Cent of Total |
| TOTAL | $7.4 \pm 0.12$ | 100.0 | $7.1 \pm 0.17$ | 0.01 | 100.0 | $6.7 \pm 0.12$ | 0.001 | 100.0 | $7.2 \pm 0.11$ | 0.1 | 100.0 |
| Sum of Primary Fractions | $7.3 \pm 0.10$ | 98.7 | $7.0 \pm 0.12$ | | 98.5 | $6.6 \pm 0.13$ | | 98.5 | $7.1 \pm 0.12$ | | 98.7 |
| Fraction I + III | $1.3 \pm 0.04$ | 17.6 | $1.5 \pm 0.11$ | 0.01 | 21.1 | $1.3 \pm 0.05$ | 1.0 | 19.4 | $1.8 \pm 0.08$ | 0.001 | 25.0 |
| Fraction II | $0.9 \pm 0.04$ | 12.2 | $1.0 \pm 0.04$ | 0.01 | 14.1 | $0.8 \pm 0.05$ | 0.05 | 11.9 | $1.2 \pm 0.06$ | 0.001 | 16.7 |
| Fraction IV + V | $4.9 \pm 0.06$ | 66.2 | $4.3 \pm 0.11$ | 0.001 | 60.5 | $4.3 \pm 0.08$ | 0.001 | 64.2 | $3.8 \pm 0.07$ | 0.001 | 52.8 |
| Albumin Fraction IV + V | $4.0 \pm 0.07$ | 54.0 | $3.9 \pm 0.10$ | 0.1 | 54.9 | $3.8 \pm 0.05$ | 0.001 | 56.7 | $3.4 \pm 0.07$ | 0.001 | 47.2 |

*Including the Standard Error of the Mean.

with a low isoelectric point, pH 1.8, and a high degree of solubility. The four primary fractions account for 96.3 per cent of the total plasma glycoprotein, the difference being due to losses during the fractionation process.

The distribution of the *plasma proteins* (Table 2) showed 66 per cent to be in Fraction IV + V and the albumin therein comprised 54 per cent of the total plasma. The total glycoprotein forms 1.5 per cent of the total plasma protein (Table 3) with Fraction VI having a ratio of 6.5 per cent due to the presence of orosomucoid with a hexose content of 17 per cent. The high hexose content of 2.9 per cent in Fraction I + III may be due to the presence of alpha-globulin which represents 17 per cent of the protein content.

*Important Factors:* The clinical features which had a significant relationship to the total plasma protein, glycoprotein, or seromucoid included (1) the extent of the disease, (2) degree of exudation of the disease, (3) cavitation present, (4) roentgen estimate of the activity of the disease process, and (5) the clinical estimate of the activity of the disease. No significant relationships were noted between the glycoprotein values and the blood counts, sedimentation rates, bacteriology, age, or sex. No effect was noted with the specific tuberculosis drugs or surgical procedures except indirectly by their influence on the activity of the tuberculous process as a whole.

*National Tuberculosis Association Extent of Disease:* (Tables I and II). The minimal cases showed normal values for total glycoprotein, seromucoid, and total protein. The moderate group showed elevated glycoprotein and seromucoid in only 5 per cent of the cases. The far advanced group showed increased total glycoprotein in 90 per cent and increased seromucoid in 88 per cent of the cases; the total plasma protein was elevated mildly in only nine of the cases who showed glycoprotein values above 150 mg. per 100 ml. Thus, only the far advanced cases showed significant increases.

The *distribution* of the total protein showed marked changes only in the far advanced group. Despite the normal total value, Fraction IV + V showed a decrease (chiefly albumin) and the other fractions showed a concomitant increase. The distribution of the glycoproteins showed changes only in the far advanced cases with a percentage increase in Fraction VI and a decrease chiefly in Fraction I+ III. When the glycoprotein was expressed as a *percentage* of the total protein (Table III), there were significant increases in the total glycoprotein-protein ratio in the moderate and far advanced groups. Fraction I + III showed a significant decrease in all the groups; Fraction II and Fraction VI showed no change; Fraction IV + V increased significantly in the far advanced group.

Inasmuch as the most extensive changes in the fractions occurred only in the far advanced group further evaluation on a clinical basis was carried out using only those chemical determinations readily available in the average laboratory, that is total serum glycoprotein and seromucoid.

*Degree of Exudation:* In correlating the glycoprotein and seromucoid values with the degree of exudation, the following results were obtained:

| Degree of Exudation | Total No. of Points | Elevated Total Glycoprotein | Elevated Seromucoid | Per Cent Elevated |
|---|---|---|---|---|
| Mild | 28 | 4 | 4 | 14 |
| Moderate | 12 | 8 | 8 | 67 |
| High | 7 | 6 | 6 | 85 |
| | 47 | | | |

Thus, the greater the degree of exudation the greater the number of patients showing elevated glycoprotein and seromucoid values.

*Cavitation:* The total diameter of the cavities present was correlated with the total glycoprotein and seromucoid values as follows:

| Total Diam. | No. Patients With Cavities | Mean Total Glycoprotein Values | Mean Seromucoid Values |
|---|---|---|---|
| Up to 4 cm. | 7 | 117 mg. per cent | 12 mg. per cent |
| 4 cm. to 8 cm. | 11 | 138 | 16 |
| Over 8 cm. | 9 | 158 | 25 |

Thus, the greater the degree of cavitation, the higher the total glycoprotein and seromucoid values. This was especially true in the far advanced cases with cavities over 4 cm. in diameter. In the moderately advanced cases, there were four cavities associated with normal values.

*Percentage of Lung Involvement:* When a correlation was attempted between the glycoprotein values and the percentage of tuberculous involvement of the lungs no clear-cut relationship could be noted probably due to the fact that, in the extent so estimated, the diseased areas included all degrees of pathological activity. However, when the degree of involvement was graded according to the pathological character of the disease a definite relationship was present. This feature was especially true of exudative disease, the most active element of the tuberculous process, as follows:

| Exudation | Per Cent Lung Involvement | Mean Total Glycoprotein Value mg/100 ml. | Mean Seromucoid Value mg/100 ml. |
|---|---|---|---|
| Mild | Up to 15 | 104 | 9 |
| | 20 to 30 | 125 | 13 |
| Moderate | Up to 20 | 106 | 10 |
| | 25 to 35 | 131 | 13 |
| | 40 to 70 | 148 | 19 |
| High | 15 | 122 | 11 |
| | 20 | 150 | 21 |
| | 35 | 160 | 26 |
| | 50 | 172 | 28 |

Thus, an analysis of the table shows: (1) that in each exudative group the greater the extent of the disease, the greater was the total glycoprotein and seromucoid values, (2) that the greater the degree of exudation, the higher were the total glycoprotein and seromucoid values for corresponding percentage involvement; the mild and moderate degrees of exudation gave similar results but the high degrees of exudation gave much higher values, (3) that the total glycoprotein and seromucoid values showed roughly parallel increases with a somewhat higher percentage increase for the seromucoid.

*Roentgen Estimate of Activity:* The degree of roentgen activity as judged by the method previously described was correlated with the total glycoprotein and seromucoid values as follows:

| Degree of Activity | Mean Total Glycoprotein Values mg/100 ml. | Mean Seromucoid Values mg/100 ml. |
|---|---|---|
| Low | 102 | 9 |
| Moderate | 111 | 11 |
| High | 151 | 21 |

Thus, the low and moderate degrees of activity gave normal values but the high degrees gave markedly elevated values. The percentage increase of the seromucoid values are somewhat greater than the total glycoprotein.

*Clinical Estimate of Activity:* Here, the findings were similar to those seen above with the roentgen estimate of activity. Only the high degrees of activity showed elevated total glycoprotein and seromucoid values.

| Degree of Activity | Mean Total Glycoprotein Values mg/100 ml. | Mean Seromucoid Values mg/100 ml. |
|---|---|---|
| Low | 107 | 10 |
| Moderate | 107 | 10 |
| High | 145 | 19 |

As noted, only the cases showing high clinical degrees of activity showed elevated total glycoprotein and seromucoid values. A similar tabulation was made comparing the primary fractions with the clinical estimation of activity and a distribution comparable to the National Tuberculosis Association classification was found (Tables I, II, III).

Abnormally elevated total glycoprotein and seromucoid values were found related to the following factors:

1. Extent of the disease—the minimal cases showed normal values, the moderate an elevation in a small number, and the far advanced an elevation in 90 per cent.
2. Degree of exudation—the more intense the degree of exudation, the greater the number of patients showing elevated values. The mild

degrees showed elevation in 14 per cent, the moderate in 67 per cent, and the high in 85 per cent.

3. Degree of cavitation—the glycoprotein values were elevated in 74 per cent of the patients with cavities, and the greater the cavitation the greater was the increase. The factor of cavitation may be regarded as a factor of both extent and degree of exudation.
4. Only the high degrees of roentgen and clinical activities of the disease showed abnormally high values.

It appears that the abnormally high total glycoprotein and seromucoid values are a manifestation of the systemic or general toxicity or protein disturbance caused by the tuberculous process. If the disease is mildly active from a systemic standpoint, then there may be no changes from normal in the protein bound carbohydrate; if the disease is moderately active systemically, there may be moderate total glycoprotein changes; and if highly active, there may result profound changes. This hypothesis is further supported by the fact that the increased values found appeared to be related to the combination of the degree of exudation present and the extent of the disease, the two most important elements producing systemic toxicity in pulmonary tuberculosis.

*Practical Applications:* As with all laboratory procedures, the clinical application of the total glycoprotein determinations is of great importance. It has been shown that in this group of known active cases of pulmonary tuberculosis, abnormal total glycoprotein values were found chiefly in the far advanced cases, the more exudative cases, the cavitary cases, and in those showing high degrees of roentgen and clinical activity. However, those showing disease of lesser extent, productive and fibroid disease, and

TABLE III

TOTAL PLASMA GLYCOPROTEIN AS PER CENT OF PROTEIN

| Classification | Normal | Minimal | | Moderately Advanced | | Far Advanced | |
|---|---|---|---|---|---|---|---|
| Number of Cases | 20 | 7 | | 20 | | 26 | |
| Component | Mean* Per Cent | Mean* Per Cent | P | Mean* Per Cent | P | Mean* Per Cent | P |
| TOTAL | 1.5 ± 0.03 | 1.5 ± 0.08 | 1.0 | 1.6 ± 0.03 | 0.01 | 2.0 ± 0.05 | 0.001 |
| Fraction I + III | 2.9 ± 0.07 | 2.5 ± 0.17 | 0.001 | 2.5 ± 0.06 | 0.001 | 2.6 ± 0.06 | 0.001 |
| II | 1.4 ± 0.04 | 1.3 ± 0.10 | 0.1 | 1.4 ± 0.05 | 1.0 | 1.3 ± 0.06 | 0.2 |
| IV + V | 0.8 ± 0.03 | 0.9 ± 0.07 | 0.2 | 0.9 ± 0.04 | 0.1 | 1.4 ± 0.06 | 0.001 |
| VI | 6.5 ± 0.82 | 7.0 ± 1.58 | 0.6 | 7.0 ± 0.94 | 0.6 | 8.0 ± 0.79 | 0.1 |

*Includes the Standard Error of the Mean.

the lower degrees of roentgen and clinical activity were usually associated with normal values.

It can therefore be stated that this test is not a good one to detect early or moderately active tuberculosis. For this purpose, bacteriological and serial roentgen studies are superior. Nor does this test apply specifically to tuberculous infection but shows increased values in many other pathologic processes which must therefore be ruled out before applying its results in evaluating both a possible diagnosis of tuberculosis, and the activity in a known tuberculosis patient. It is therefore a rather crude index of activity in clinical tuberculosis. This feature was demonstrated in another way: after inspection of x-ray films only, a roentgen estimate was made of the probable total glycoprotein value and compared with the actual determinations:

| Total Glycoprotein Values | Number of Cases | Roentgen Estimate | | Correct Prediction of Per Cent |
|---|---|---|---|---|
| | | Normal | Elevated | |
| Normal | 29 | 25 | 4 | 86 |
| Elevated | 23 | 4 | 19 | 82 |

However, total glycoprotein determinations may be of great clinical value under other circumstances. It often happens that all the usual studies fail to disclose whether a tuberculous lesion is active or inactive and here the glycoprotein determinations may be of importance. It may be of much greater value in non-pulmonary tuberculous disease than in pulmonary for bacteriological and roentgen studies are often less informative of the clinical status of the lesion and the glycoprotein studies may be correspondingly more instructive. Further work along this line is contemplated in tuberculous disease of such systems as the lymph nodes, meninges, kidneys, and bones. The importance of the glycoprotein determinations is being studied currently with regard to its prognostic value: granted that a tuberculous process is active, a persistently high or rising glycoprotein value may be of serious import whereas a falling value may show a favorable clinical response.

## SUMMARY

1. The plasma content of protein and the protein-bound carbohydrates was determined in 53 patients with active pulmonary tuberculosis and 20 normal individuals. Their concentration was also determined in each of the four primary fractions of plasma isolated by the use of the low temperature-low salt-ethanol procedure of Lever.

2. The values of the total glycoprotein and seromucoid fractions were correlated with a number of clinical factors and were found to increase with the extent of the disease, the extent of cavitation, the degree of exudation, the roentgen estimate of activity, and the clinical estimate of ac-

tivity. The increased values appear to be a manifestation of the systemic effect of the disease process.

3. The practical application of these chemical determinations is discussed and it is felt that they have a minor but definite place in the diagnosis of pulmonary tuberculosis or in estimating the degree of activity. However, their value in prognosis, in management of the disease, and in non-pulmonary tuberculous disease remains to be determined.


## RESUMEN

1. Se determinó el contenido de proteina y de los carbohidratos ligados a proteínas en 53 enfermos con tuberculosis pulmonar activa y en 20 individuos normales. La concentración fué también determinada en cada una de las cuatro fracciones primarias de plasma aislado por el uso del procedimiento de Lever de la baja temperatura-baja sal-etanol.

2. Los valores de la glicoproteína total y las fracciones seromucoides se correlacionaron con un número de factores clínicos y se encontró que aumentaban con la mayor extensión de la enfermedad, la mayor extensión de la excavación, el grado de exudación, la estimación radiológica de la actividad, así como la estimacién clínica de esta última. El aumento de los valores parece ser debido a un efecto general del padecimiento.

3. La aplicación práctica de estas determinaciones clínicas se discute y se cree que tienen un lugar menor pero definido en el diagnóstico de la tuberculosis pulmonar y en la valudación de la actividad.

Sin embargo, su importancia para el pronostico, el tratamiento y en comparación con la tuberculosis no pulmonar, está por determinarse.



## ZUSAMMENFASSUNG

1. Der Plasmagehalt von Eiweiss und an Eiweiss gebundenen Kohlehydraten wurde bei 53 Kranken mit aktiver Lungentuberkulose und 20 normalen Personen bestimmt. Es erfolgte auch eine Bestimmung von deren Konzentration für jede der 4 primären Plasmafraktionen nach Isolierung unter Verwendung der Tief-Kühl-Salz-Aethylalkohol-Methode von Lever.

2. Die Werte der gesamten Glycoprotein—und Mucidan-Serum-Fraktionen wurde in Beziehung gesetzt zu einer Anzahl klinischer Faktoren, und es fand sich eine Zunahme zugleich mit der Ausdehnung der Erkrankung, dem Grad der Cavernenbildung, dem Ausmass der Exsudation, der röntgenologischen Abschätzung der Aktivität und der klinischen Bewertung der Aktivität. Die erhöhten Werte scheinen eine Manifestation der Allgemeinwirkung des Krankheitsprozesses zu sein.

3. Besprechung der praktischen Anwendung dieser chemischen Bestimmungen; es wird zum Ausdruck gebracht, dass sie einen untergeordneten, aber bestimmten Platz bei der Diagnose der Lungentuberkulose haben oder bei der Abschätzung des Aktivitätsgrades. Ihr Wert für die Prognose,

Betreuung der Krankheit und extrapulmonale Tuberkulose muss allerdings noch bestimmt werden.

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# Incidence of Chronic Pulmonary Disease Among Patients with Esophageal Disorders

JOSEPH R. VIVAS (Col.), MC*, and EDDY D. PALMER (Lt. Col.), MC**
Washington, D. C.

It is well known that chronic pulmonary disease is a threat to patients who have an esophageal lesion which causes esophageal retention or transcardial reflux.[1-7] The conditions which have aroused most interest in this respect are achalasia, diverticulosis, chalasia, hiatus hernia, esophageal foreign body, and stricture. The mechanism of pulmonary involvement seems to be merely that of periodic unrecognized transadital aspiration of material from the esophagus. Presumably, this is largely a nocturnal affair, or at least recumbency favors migration of esophageal contents toward the pharynx. The tone of the cricopharyngeus muscle can be given credit for precluding the danger of massive aspiration. The special danger of Zenker's diverticulum lies in the fact that this is a hypopharyngeal pouch with its stoma lying superior to the cricopharyngeus muscle.

The severity of pulmonary disease encountered in some instances of achalasia and of esophageal diverticulosis has been disturbing, and we believe that more information is needed on the incidence of both clinical and subclinical pulmonary disease in all esophageal abnormalities, both those of a retentive nature and causing dyskinetic effects. For the most part, the experiences of others have been recorded in terms of extant pulmonary disease rather than the potential threat of pulmonary disease.

## *Material and Methods*

The records of inpatients discharged from this hospital during the calendar year of 1954 with diagnoses which included an esophageal disease were reviewed. Those with esophageal varices only were not included. There were 68 in this series. In order to include patients whose illness was not serious enough to require hospitalization, 32 additional outpatient records were selected at random to bring the total number to 100. Although it was recognized that a cause and effect relationship could not be proved, the purpose of the investigation was to determine the incidence of pulmonary disease among these patients by examination of the records and roentgenograms.

There were 65 men and 35 women in the group. All were Caucasians, except for 10 Negroes. Their ages varied from 12 months to 89 years. The number per age-decade, from the first through the ninth decades, were, respectively, 4, 4, 22, 17, 19, 18, 8, 6, and 2.

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*Director of Graduate Education, Walter Reed Army Hospital. Presently Chief, Department of Medicine, Madigan Army Hospital, Tacoma, Washington.

**Chief, Gastroenterology Service, Walter Reed Army Hospital.

*Findings*

The incidence of observed pulmonary diseases in relation to the esophageal diseases represented is shown in Table I. Both the esophageal and pulmonary diseases were chronic in all cases, but there was great variation in the duration of clinical manifestations. In some, particularly those with a diverticulum, the esophageal lesion was encountered unexpectedly during contrast fluoroscopy for some unrelated complaint. It is never possible to know when a diverticulum has its inception, when achalasia first becomes responsible for esophageal retention, or how frequently esophagitis may lead to dyskinesia sufficient to encourage reflux. For this reason, it was not propitious to make estimations of how long the possibility or threat of pulmonary aspiration had existed in these patients.

All of the pulmonary diseases noted in this report are of the type which might be caused by repeated transaditai aspirations (Table II). Other conditions, such as emphysema, were eliminated from consideration as not pertaining to the discussion. No correlation could be found between the types of esophageal disease and the specific types of secondary pulmonary complication. The final common pathway was unquestionably a simple relative obstruction with repeated aspiration, except as certain esophageal dis-

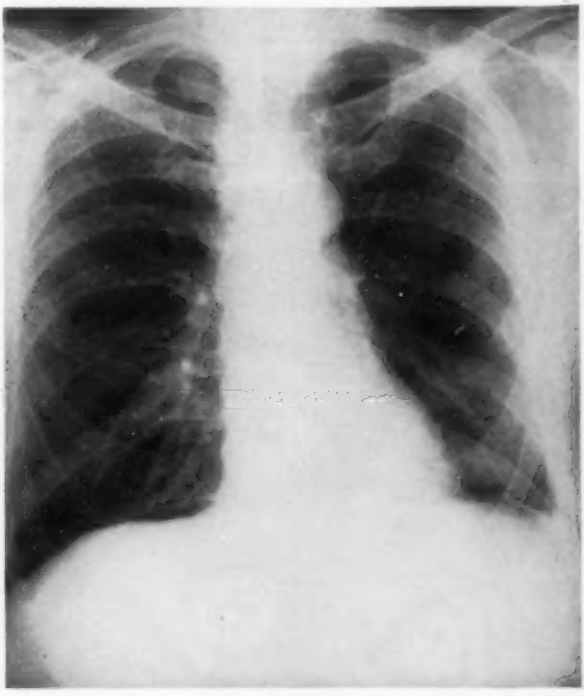

FIGURE 1

TABLE I

DISTRIBUTION OF ESOPHAGEAL DISEASES AMONG 100 PATIENTS STUDIED FOR PULMONARY DISEASE

| Esophageal Disease | Number of Patients | Patients With Chronic Pulmonary Disease |
|---|---|---|
| Hiatus Hernia Without Secondary Esophageal Change | 42 | 2 |
| Diverticulum of Esophagus | 13 | 4 |
| Subacute Erosive Esophagitis Without Hiatus Hernia | 12 | 2 |
| Achalasia | 8 | 6 |
| Subacute Erosive Esophagitis With Hiatus Hernia | 7 | 3 |
| Stricture, Secondary to Esophagitis | 6 | 0 |
| Stricture, Congenital | 3 | 0 |
| Carcinoma of Esophagus | 3 | 2 |
| Zenker's Diverticulum | 3 | 1 |
| Corrosive (Lye) Stricture | 2 | 2 |
| Radiation Stricture | 1 | 0 |

FIGURE 2A

FIGURE 2B

TABLE II

INCIDENCE OF PULMONARY DISEASES

| | |
|---|---|
| Chronic Bronchitis | 8 |
| Recurrent Pneumonia | 9 |
| Chronic Pulmonary Fibrosis | 1 |
| Bronchiectasis | 1 |
| Lung Abscess | 1 |
| Pneumothorax Due to Perforation | 1 |
| Empyema Due to Perforation | 1 |

eases were more likely to cause pleural diseases through perforation than were others.

*Case 1:* This 57 year old white man had had a bleeding gastric ulcer two years previously, and was hospitalized because of intractable nausea, vomiting, and midepigastric pain. Prior to his present symptoms he had noticed that food stuck in the lower part of his esophagus and in the early morning he tasted hot secretions coming from the stomach. Three weeks before the onset of his present illness, he had had an acute respiratory infection diagnosed as left lung pneumonia which he had considered an aggravation of the chronic bronchitis which had been present for two years. Physical examination was within normal limits for a man of his age except for scattered coarse rales in both lung bases. X-ray film of the chest (Fig. 1) revealed a slight shift of the mediastinum to the left. The right lung field was clear. The left lung base showed evidence of a recent pleural reaction with obliteration of the left costal angle. Esophagoscopic examination showed severe erosive esophagitis and roentgenologic study again revealed active gastric ulcer. Subtotal gastrectomy was performed. Although dyspepsia cleared, dysphagia persisted. Repeat esophagoscopic examination three months postoperatively showed no change in the esophagitis.

*Case 2:* This 88 year old Negro man was hospitalized because of nausea, vomiting, a sensation of precordial burning discomfort, and pain in the left side of the chest. He had a history of chronic bronchitis with repeated exacerbations during the previous

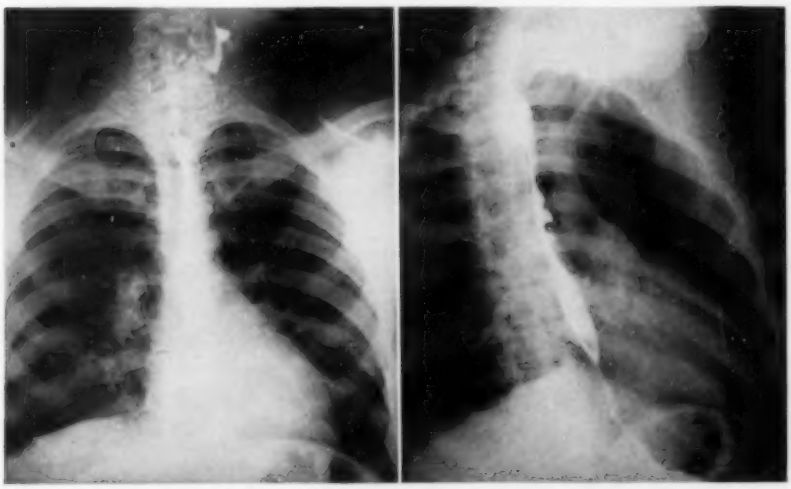

FIGURE 3A FIGURE 3B

five years. Physical examination revealed a thin, emaciated, anxious elderly man. His temperature was 100° F., pulse, 80, blood pressure, 140/80, and the abdomen was normal. Chest examination revealed many rales and rhonchi. He was given intravenous terramycin and liquids by mouth. After two days he became asymptomatic. Upper gastrointestinal fluoroscopy and x-ray films revealed a midthoracic esophageal diverticulum (Fig. 2A). Repeat chest films made in March and April 1954 read as follows: Heart not enlarged; great vessels somewhat elongated and sclerosed. Right lung field appeared normal. Left lung field showed dense infiltration of the lower half of the lung; suggestion of mediastinal displacement to the left. The films were suggestive of aspiration pneumonitis (Fig. 2B). Because of his age, no surgical treatment was undertaken.

*Case 3:* Physical examination of this 20 year old man patient revealed a heart murmur, and electrocardiograph studies showed some abnormalities. He complained of burning sensations of the precordial area. History revealed that as a child he had had mild asthma. Otherwise he had been a rather athletic individual, except for repeated episodes of pulmonary congestion and bronchitis of the right lung which he had experienced during the past few months. A diagnosis of possible congenital abnormality of the coronary arteries was suspected. He was 5′ 10″ tall and weighed 160 pounds. His pulse was 76 and his blood pressure, 120/80. His general appearance was that of a well developed, young, muscular Negro. A slight systolic murmur, rough in quality, was heard at the sternal border in the third left intercostal space. Examination of the lung field showed multiple crackling rales in the right base. There was evidence, by chest x-ray film, of a diffused infiltrative process in the right lung with marked prominence of the bronchovascular marking in the right base (Fig. 3A). Studies failed to confirm the suspicion of cardiac disease. An esophageal diverticulum was discovered on x-ray film (Fig. 3B). It was felt that the precordial symptoms, the burning sensation of the esophagus, and the repeated pulmonary infections were the result of his esophageal diverticulum.

*Case 4:* This 63 year old white man had been in excellent health until six weeks prior to initial study when he noticed slight difficulty in swallowing. Food began to stick in the lower part of the chest. Dysphagia gradually became more severe. At the same time he developed pulmonary complaints in the form of chronic bronchitis with increased expectoration during the early morning hours. Physical examination showed a fairly well nourished white man; there were coarse rales in the bases of both lungs. The heart was within normal limits. X-ray films of the chest made in 1954 and 1955 showed chronic pulmonary disease with patchy infiltrations and evidence of repeated pleural reactions. A 1955 film showed evidence of contrast media aspiration into the lungs after barium swallow studies (Fig. 4). Esophagoscopy was performed repeatedly. Slight dilatation of the lower third of the esophagus was found, but there was no ulceration or obstruction. As a result of a biopsy, a diagnosis of squamous

FIGURE 4

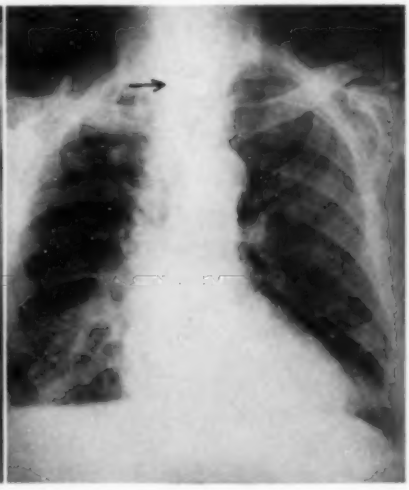

FIGURE 5

cell carcinoma of the esophagus was made. In March 1954 he had extensive esophageal resection with the stomach being fastened to the proximal esophagus at the level of the arch of the aorta. He developed stenosis at the site of anastomosis, which necessitated repeated dilatations. In January 1955, a portion of small bowel, which had herniated into the chest cavity, and a gangrenous section of the small bowel were removed. Esophageal stenosis became more pronounced following surgery, which necessitated additional dilatations.

*Case 5:* This 70 year old white man was hospitalized because of frequent tarry stools. Prior to admission, his health had been good except for the development of chronic bronchitis with early morning expectoration and two previous episodes of melena. On previous visits to the outpatient clinic a diagnosis of Zenker's diverticulum of the esophagus and hiatus hernia had been established. When examined, he was obese and extremely pale. His temperature was 98.7° F., his pulse, 110 and blood pressure, 110/60. His chest was emphysematous in configuration and loud rhonchi were heard in both bases. The heart did not appear enlarged. The rectum contained a quantity of black tarry stools. X-ray film of the chest showed the heart to be enlarged. There were extensive sclerotic changes in the great vessels. The spine showed slight scoliosis to the right. There were diffused infiltrations of both bases of the lung fields. A stomach tube was in place and there was evidence of diverticulum of the esophagus at the level of the third dorsal vertebra (Fig. 5). He had a stormy hospital course and became combative and disturbed, possibly because of cerebral anemia. However, the second day after admission there was no further evidence of bleeding. Diagnosis of duodenal ulcer was established by x-ray.

*Case 6:* This 46 year old white man was hospitalized because of ascites and edema of both extremities and pulmonary infiltration. Past history revealed fatigue of two months' duration and mild ascites for about one month. The patient had been drinking a fifth of whiskey a day for the past 15 to 20 years. Physical examination showed marked ascites, 4-plus pitting edema of the legs, and spider angiomata over the shoulders, face, and upper abdomen. There was no abnormal heart finding. Many coarse rales were heard in both lung bases. X-ray films of August 17 were suggestive of localized atelectatic processes (Fig. 6A). On August 26, his temperature rose to 103.6° F., and he became cyanotic and dyspneic. An x-ray film of the chest revealed an infiltration of the right upper lung field which was suspected as being an aspiration pneumonia. During his acute pulmonary complication, the patient experienced massive hematemesis for the first time and required many blood transfusions. All laboratory studies suggested that the liver condition was due to cirrhosis. In September, x-ray films of the chest revealed a round infiltration, 3 cm. in diameter, in the right lung field, suggestive of lung abscess (Fig. 6B). Because of the lack of response in his pulmonary condition, bronchoscopy was performed, but no abnormality was found. Esophagoscopy revealed a severe erosive esophagitis. He continued a downhill course and died December 3, 1954. Postmortem examination revealed evidence of severe Laennec's cirrhosis, abscess of the right lung, severe chronic esophagitis, and hiatus esophageal hernia.

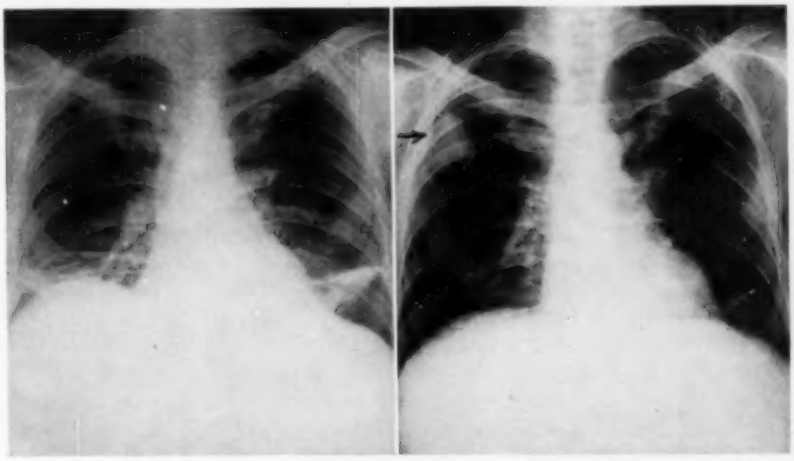

FIGURE 6A FIGURE 6B

SUMMARY

A study of 100 patients with esophageal pathology has been presented. Twenty-two patients had chronic pulmonary disease. This study was undertaken not to prove cause and effect relationship, but to bring out the high incidence of transadital aspiration type of pneumonitis in esophageal disease.

RESUMEN

Se presenta un estudio de 100 enfermos con patología del esófago. Veintidós de los enfermos tenían una enfermedad pulmonar crónica. Este estudio se emprendió no para demostrar relación de causa a afecto, sino para evidenciar la elevada frecuencia del tipo de neumonitis por aspiración transadital.

RESUME

Les auteurs présentent une étude sur 100 malades atteints d'affections oesophagiennes. 22 malades présentaient des manifestations pulmonaires chroniques. Cette étude fut entreprise non pour prouver un rapport de cause à effet, mais pour mettre l'accent sur la fréquence élevée des atteintes pulmonaires par aspiration dans les affections oesophagiennes.

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# Diagnostic Surgical Procedures for Pulmonary Disease: Review of a Two-Year Experience

H. PAUL LONGSTRETH, Major, MC, AUS, F.C.C.P.**; JULIO C. DAVILA, Captain, MC, AUS*; and ELMORE M. ARONSTAM, Lt. Colonel, MC, USA*

Phoenixville, Pennsylvania

A definitive diagnosis of pulmonary disease cannot be made, in a significant number of cases, without the employment of certain surgical procedures. A presumptive diagnosis may be reached with the aid of skin tests for tuberculosis, histoplasmosis, coccidioidomycosis, and blastomycosis, sputum smear and culture examinations for various organisms, fungal serological tests, and bronchoscopic study with cytologic and bacteriologic investigations of aspirated secretions as well as roentgenography. Not infrequently some of the positive results are not related to the disease under investigation and may lead to a false diagnosis and possibly misdirected therapy.

A number of surgical procedures, aimed at diagnosis,[1-8] have been employed in recent years in problem chest cases. These include lung biopsy, scalenus or paratracheal fat pad biopsy, pleural and pericardial biopsies, and exploratory thoracotomy. Today, these operations can be done with considerable safety as a result of improvements in the techniques of thoracic surgery, anesthesia, and pre- and post-operative management.

The authors have employed lung biopsy when dealing primarily with diffuse pulmonary disease. Disseminated lung lesions caused by pneumoconiosis, tuberculosis, sarcoidosis, histoplasmosis, coccidioidomycosis, blastomycosis, moniliasis, and various types of malignancy frequently produce identical roentgenographic signs. In such cases, direct study of a representative section of lung tissue is essential in order to arrive at a correct diagnosis.

To obtain a lung biopsy, in general, an intercostal incision is made anteriorly or laterally over a representative area. General endotracheal anesthesia is used instead of local, as recommended by Klassen[2]. If need arises to enlarge the incision, it is much simpler to do so under general anesthesia. This type of anesthesia allows much more adequate exploration of the area in question and permits biopsy of as many areas as may be suspected.

Daniels[6] described a method for the removal of the scalenus or paratracheal fat pad and lymph nodes as a useful adjunct in the diagnosis of certain intra-thoracic, pulmonary, or mediastinal diseases. Several reports have been published recommending its employment.[1, 6] Favorable aspects of this surgical procedure are that it can be done under local anesthesia, it requires but a few minutes and, in skilled hands, it is associated with no morbidity. This operation can be performed, therefore, on elderly and poor surgical risk patients without untoward effects.

Recently, biopsy of the pleura has been advocated[7, 8] in undiagnosed

From the Pulmonary Disease Service** and the Thoracic Surgical Service,* Valley Forge Army Hospital.

pleurisies, especially in patients in the cancer age. It is imperative to establish the etiology of the pleural condition in cases in which the cultures of the pleural fluid have failed to grow out an organism. Sutliff, Hughes, and Rice[8] reported on 21 patients in whom pleural biopsies were done. Seventeen were interpreted as being tuberculosis although positive cultures were obtained in only six of nine cases examined. In the remaining cases, the diagosis of tuberculosis was based on the microscopic demonstration of tubercle bacilli. Three had pleurisy secondary to carcinoma. In two of these, the biopsy of the pleura showed malignant cells, but the third one revealed non-specific inflammation. A repeat bronchoscopy showed bronchogenic carcinoma. Blastomyces dermatitidis was recovered on culture of a co-existing skin lesion in the twenty-first case. The biopsy in this case showed yeast-like organisms in the tissue that was the site of a polymorphonuclear and granulomatous reaction.

Small and Landman[7] reported on five cases of pleural biopsy in which the etiology of the effusion could not be established by bacteriological methods. All of them were said to be tuberculosis, histologically.

Pericardial biopsy is another surgical procedure which can be used in an attempt to establish a definitive diagnosis. This has become extremely important in view of the specific anti-tuberculous drugs and the steroids which we have today.

Diagnostic thoracotomy has been employed when dealing with an undiagnosed, unilateral pulmonary lesion and performed early if suspected of being malignant. This surgical procedure has attained wide acceptance and popularity because early extirpation of a malignant lesion is imperative if a cure is to be realized. If the lesion is not malignant, accurate diagnosis and effective treatment can be accomplished.

In those cases with diffuse pulmonary lesions of undetermined etiology, pulmonary biopsy proved to be of extreme value in establishing a diagnosis and determining specific therapy, prognosis, and disposition. This procedure was carried out in 16 cases at the Valley Forge Army Hospital during the past two years. Four were eosinophilic granuloma, four sarcoid, three interstitial fibrosis, one anthrasilicosis with tuberculosis, and one histoplasmosis. One of the eosinophilic granuloma cases was thought to be metastatic carcinoma pre-operatively. The foreign body granuloma cases were strongly suspected of being sarcoid prior to surgical intervention. One of these gave a history of exposure to Kapok dust, another had worked in a fur processing plant as a sweeper; the history of the third case was negative.

The scalenus fat pad biopsy was quite disappointing in our series of 27 cases in which it was performed. Eleven revealed histologically hyperplastic lymphadenopathy, seven were granuloma compatible with tuberculosis or sarcoid, one was Hodgkin's Disease, one tuberculosis. In six, normal lymphatic and fatty tissue was found and one showed fat necrosis. Our results differed considerably from those reported elsewhere and a second operation, exploratory thoracotomy with pulmonary biopsy, had to be performed to establish a definitive diagnosis.

Pleural biopsy was equally disappointing in 10 cases in which we were unable to reach a diagnosis clinically by means of pleural fluid cultures and allied non-surgical procedures. Nine of the biopsies revealed chronic organizing pleuritis of unknown etiology, and the 10th simulated pleural mesothelioma. Cultures in all instances were negative. Reports in the recent literature[7, 8] are exceptionally encouraging but do not coincide with our results. The failure of this procedure was most disappointing. The problem of specific diagnosis in pleural effusions remains unsolved since findings of non-specific inflammation on histologic examination and of negative bacteriology contribute nothing toward rational management of these cases. One must still be extremely cautious with a non-specific histologic picture.

Pericardial biopsies were done in four cases of pericarditis of unknown etiology. The histological diagnosis was chronic organizing pericarditis of unknown etiology. The cultures of the specimens were all negative. It was felt that these four pericarditic cases probably represented a rheumatic inflammatory process.

Our most favorable results were obtained in the diagnostic thoracotomy group which consisted of 36 cases. Eight were proved to tuberculosis, Table I, and proper chemotherapy was initiated in all cases with excellent results. Four were carcinoma, and appropriate surgery was carried out. The six histoplasma cases were soon discharged to active duty. The procedure made possible avoidance of prolonged hospitalization and treatment of these patients as tuberculosis.

There has been no mortality or morbidity in the 93 procedures in this series. It is the current opinion of the authors that the safety of surgical diagnostic procedures has made mandatory their early use in cases which cannot be specifically diagnosed by other means. The "wait and see" attitude long practiced widely is no longer justifiable.

By these means, the need for rationally planned and promptly instituted specific medical treatment can usually be ascertained. The questions of communicability of an infectious disease (i.e., tuberculosis), of the patient's peace of mind, rehabilitation, and of the disposition of a case in the military service can be settled promptly.

The surgical diagnostic procedure should be individualized for each given problem. In general, however, the most satisfactory results, in our hands, have been obtained with thoracotomy which permits adequate exploration and biopsy of any suspected structures.

TABLE I—DIAGNOSTIC THORACOTOMY (Thirty-six Cases) 1954-1955

| | | | |
|---|---|---|---|
| Tuberculosis | 8 | Hamartoma | 1 |
| Carcinoma | 4 | Diaphragmatic Hernia | 1 |
| Histoplasmosis | 6 | Chondrosarcoma | 1 |
| Coccidioidomycosis | 3 | Bronchogenic Cyst | 1 |
| Chronic Pneumonitis | 1 | Paracardiac Lipoma | 1 |
| Undiagnosed Granuloma | 5 | Neurofibroma | 1 |
| Chronic Lung Abscess | 1 | Thymoma | 1 |
| Cystic Disease | 1 | | |

The authors favor a lateral incision over the fifth or sixth rib, entering the pleural cavity through an interspace and opening the thorax sufficiently to allow manual exploration. A decision is then made as to whether further extension of the incision is necessary. In pleural disease, decortication may be deemed advisable at this time. In granuloma, one or more lesions can be removed safely by wedge resection. Frozen section may further aid in the surgical management of the case.

SUMMARY

1. It is imperative to establish the diagnosis in undetermined pulmonary lesions and to resort to one of several diagnostic surgical biopsy procedures, providing the clinical aids of fungal and tuberculin skin tests, smears and cultures of sputums, gastric washings, aspirated bronchial secretions and of material from pleural and pericardial cavities, as well as fungal serological studies have been of little or no value.

2. Diagnostic thoracotomy has proved to be of the greatest value in the authors' experience. It should not be delayed unnecessarily. It can be done with considerable safety.

3. Fat pad, pleural and pericardial biopsies did not aid in the determination of the etiology of the underlying disease in the majority of our cases. These results differ greatly from those reported in the medical literature.

4. One can save the patient, with undiagnosed pulmonary disease, considerable inconvenience and may better his prognosis, by earlier surgical intervention. The practice of "watchful waiting," which is still quite prevalent, is no longer justifiable.

CONCLUSIONES

1. Cuando los estudios clínico, las pruebas cutáneas con tuberculina y productos micósicos, frotis y cultivos, de esputos, lavado gástrico, secreciones bronquiales aspiradas, y material de las cavidades pleurales y pericárdica, así como estudios serológicos de micosis no han sido de valor para establecer el diagnóstico, es imperativo el recurrir a uno de los procedimientos para realizar una biopsia en los casos de lesiones pulmonares indeterminadas.

2. Según la experiencia de los autores la toracotomía diagnóstica ha demostrado ser de gran valor. No debe demorarse innecesariamente. Puede realizarse con considerable seguridad.

3. El estudio de la bola gaseosa, o las biopsias pleurales y pericárdicas no ayudaron para determinar la etiológica de la enfermedad suyacente en la mayoría de los casos neustros. Estos resultados difieren grandemente de los relatados en la literatura.

4. Pueden evitarse al paciente que tiene una enfermedad pulmonar no diagnosticada, muchas molestias y mejorar su pronóstico con una operación quirúrgica temprana. La práctica de la "vigilante espera" que aún es muy prevaleciente, no se justifica más.

RESUME

1. Dans le cas d'altérations pulmonaires de nature indéterminée, il est capital d'établir le diagnostic. A condition que les moyens cliniques: tests cutanés tuberculiniques et fungiques, frottis et cultures des expectorations, lavages gastriques, aspiration de secrétions bronchiques, et des liquides

des cavités pleurales et péricardiques, aussi bien que les études sérologiques et fongiques n'aient donné que des renseignements nuls ou très insuffisants, on peut recourir à un procédé de diagnostic par biopsie chirurgicale.

2. Selon l'expérience des auteurs, la thoracotomie exploratrice a prouvé qu'elle était le procédé qui avait le plus de valeur. On ne devrait pas attendre trop longtemps sans raison avant de l'entreprendre. Elle peut être faite avec beaucoup de sécurité.

3. Les biopsies pleurales et péricardiques ne furent d'aucun secours dans la détermination de l'étiologie de l'effection sous-jacente dans la majorité de leurs cas. Ces résultats sont très différents de ceux rapportés dans la littérature médicale.

4. On peut sauver le malade atteint d'une affection pulmonaire non diagnostiquée, améliorer considérablement son état et son pronostic, grâce à une intervention chirurgicale précoce. La pratique de l'attente avec "mise en observation" qui prévaut encore ne se justifie plus.

## SCHLUSSFOLGERUNGEN

1. Es ist eine zwingende Forderung, die Diagnose bei unbestimmten Lungenveränderungen zu klären und zu einer der verschiedenen chirurgischen Biopsie-Massnahmen zu greifen, sofern sich die klinischen Hilfsmittel bei Pilz—und Tuberkulin-Hauttesten, Ausstrichen und Kulturen von Sputum, Magensaft, aspiriertem Bronchialsekret und vom Material aus Pleura—und Pericard-Höhlen ebenso wie serologische Pilzuntersuchungen als von geringem oder keinem Wert erwiesen haben.

2. Nach der Erfahrung des Verfassers hat sich die diagnostische Thorakotomie als von grösstem Nutzen erwiesen. Sie sollte nicht unnötig hinausgezögert werden. Sie kann mit beträchtlicher Sicherheit durchgeführt werden.

3. In der Mehrzahl unserer Fälle haften Fettpolster-Pleura—und Pericard-Biopsien nicht bei der Klärung der Aetiologie der zugrundeliegenden Krankheit. Diese Ergebnisse weichen von den in der medizinischen Literatur mitgeteilten erheblich ab.

4. Man kann den Patienten mit nicht diagnostizierter Lungenkrankheit durch frühzeitigeres chirurgisches Eingreifen beträchtliche Unannehmlichkeiten ersparen und seine Prognose verbessern. Das übliche Verfahren des "wachsamen Wartens," das noch immer ziemlich vorherrscht, ist nicht länger gerechtfertigt.

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# Bronchoscopy and Television

A. SOULAS, M.D., F.C.C.P., J. M. DUBOIS DE MONTREYNAUD, M.D., F.C.C.P., R. J. EDWARDS, M.D., and A. J. GLADU, M.D.

Paris, France

A new method of bronchoscopy which utilizes a telescope equipped with a quartz rod providing a powerful light source, has made it possible to adjust a television camera directly to the endoscope. We should like to describe briefly two experiments with television which may be of interest to you.[1]

Our first experience in televising bronchoscopy directly took place in December, 1955, with the cooperation of Television Nationale. Our purpose was to relay the endoscopic views which could be obtained with the "Fourestier, Gladu, Vulmiere" apparatus. The same view of the bronchi as seen by the bronchoscopist and his assistants on the screen in the operating room could thus be followed at the same time by all those outside, on their individual television sets. The experience was valuable in that it showed us that it could be done.

As one of us has written in *Bronchology*, there may be practical, social and prophylactic interests in utilizing a national television network in this way, and there may be also the value in a particular case, in permitting a specialist to give his opinion regarding a bronchoscopy which takes place at some distance. Actually, however, because the procedure of performing a bronchoscopy for television requires so much on the part of the operator in becoming accustomed to the technique, it should naturally be reserved for exceptional cases. In this respect, the systematic taking of bronchoscopic films is a simpler and more fruitful means of insuring satisfactory consultations because it can be achieved under better conditions.

The second experiment was undertaken for pedagogical reasons; this was television in a university hospital, and reserved for the bronchoscopist and assistants, other physicians and medical students. Once again, it was a matter of adjusting the television camera to the special Fourestier, Gladu, Vulmiere bronchoscope. In this case, we did not use one of the Nationale Television cameras, but a much more practical camera which had been manufactured privately, greatly reduced in volume and weight (25 cm. long, 15 cm. wide and three lbs. in weight. The new model for which we are waiting is twice as small and twice as light.

This camera makes it possibe to transmit to the viewing screen the same image which the operator himself has, of the progression of the tube into

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1 Additional information on the subject has been reported by A. Soulas and P. Mouier-Kuhn in "*Bronchology*," Second Edition, Volume II, pp. 1092-1118; Masson and Company, Editors, Paris, 1956.

Presented at the 22nd Annual Meeting, American College of Chest Physicians, Chicago, Illinois, June 6-10, 1955.

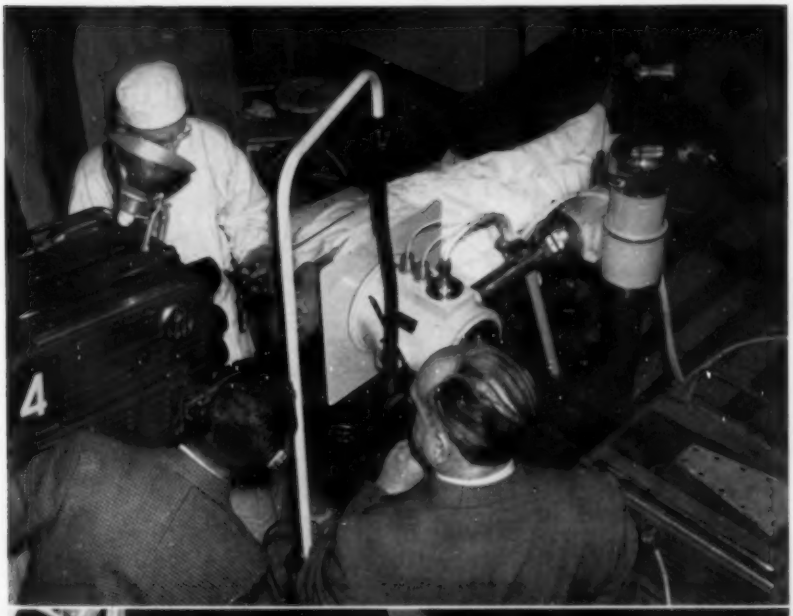

FIG. 1

FIG. 2

*Figure 1:* General arrangement. The patient and the equipment are in place. The special Fourestier, Gladu, Vulmiere camera is ready in front of the enormous National Television equipment.—*Figure 2:* The bronchoscope is in the trachea; it is adjusted to the television camera; the bronchoscopist does not look into the telescope, but at the television screen.

the bronchi. This, of course, obviates the old necessity of taking turns in looking into the tube during a bronchoscopy, when several people wish to follow it, and modifies the examination procedure and information which can be gained from it.

Moreover, the same bronchoscopic picture can be transmitted to several amphitheatres for physicians and students, at the same time that a commentary is relayed through a loud speaker. Thus a greater number of students are able to benefit from the bronchoscopic examination itself, without requiring each to look into the telescope. It is likely that the use of television only amplifies the instruction, which is doubtless given with as much profit by the bronchoscopic films.

Two applications of this procedure were made for students during the annual International Course of Broncho-esophagologie which was recently given in Paris.

The first procedure was performed on a man at Laennec Hospital, in Professor Robert Monod's Clinic for Chest Surgery. The bronchoscopic pictures of several patients were transmitted simultaneously on several screens: on one in the thoracic surgery division; on one in Professor Etienne Bernard's Pneumo-Pthisiology Service; and, of course, on the screen in the operating room. All the students and all the physicians grouped around the screen were able to observe at the same time as did the bronchoscopist, a tuberculous stenosis, a neoplastic stenosis, and the alteration of the bronchi in a bronchiectasis.

FIGURE 3: Another view of the room where the bronchoscopy is taking place. A small group of technicians, engineers, and physicians is seen who are following the bronchoscopic procedure on the screen and who listen to the accompanying explanation; all the television viewers in Paris and outlying communities were able to do the same.

The second application seemed to have an even greater importance. It permitted the viewers to observe at the same time as did the bronchoscopist and the physiologist, the bronchoscopic results of the excitation of the vagus

FIG. 4

FIG. 5

*Figure 4:* A photograph, only fair in reproduction, of one of the fine pictures obtained on the television screen. Orifice and stem of the middle lobe; below, the lower right bronchus, its divisions and their orifice.—*Figure 5:* Another photograph of a picture obtained on the television screen above, at 9-11 o'clock, the upper lobe of the left bronchus; below, the lower lobe and its divisions.

nerve, and of the administration of prostigmine and acetylcholine in an anesthetized dog. Professors and students were thus able to observe the production of a spectacular bronchial spasm. This production for the students of our course demonstrated the interest which television may have in the domain of experimental research. It took place in Dr. Halpern's laboratory in the Medical Clinic of Professor Pasteur Vallery-Radot in Broussais Hospital.

This new television procedure should be in color; that would be preferable, and is, of course, already possible in this country. Moreover, it may be used in all endoscopy, as we have done: in photo-cinematography during proctoscopy, laparoscopy, urethroscopy. The future will show the results and the value of all these various techniques, particularly in bronchoesophagoscopy.

SUMMARY

Using a new type of bronchoscope with a proximal light source, telescope and a quartz rod to transmit the light to the distal tip of instrument, sufficient illumination was obtained to permit attaching a television camera directly to the endoscope. The image was transmitted to screens in the operating room and in various services in the hospital through a closed circuit. This was found to be of great value for both teaching and consultation.

RESUMEN

Usando un nuevo tipo de broncoscopio con una fuente de luz proximal, telescopio y una varilla de cuarzo para transmitir la luz al polo distal del instrumento, se obtuvo la suficiente iluminación para permitir adaptar una cámara de televisión directamente al endoscopio. La imagen fué transmitida a pantallas en la sala de endoscopías y en varios servicios del hospital a través de un circuito cerrado. Esto resultó de gran valor educativo y de consulta.

RESUME

Utilisant un type nouveau de bronchoscope avec source lumineuse proximale, un télescope et un tube de quartz pour transmettre la lumière á l'extrémité de l'instrument, on peut obtenir une luminosité suffisante pour permettre l'adjonction à l'endoscope d'une caméra de télévision. L'image fut transmise sur les écrans de la salle d'opération et dans les différents services de l'Hôpital, en circuit fermé. Ceci est d'un grand intérêt à la fois pour l'enseignement et la clinique.

ZUSAMMENFASSUNG

Durch die Verwendung eines neuen Typs eines Bronchoskops mit einer proximalen Lichtquelle, Teleskop und einer Quarzlinse zur Übertragung des Lichtes zum distalen Ende des Instrumentes wurde eine ausreichende Beleuchtung erreicht, die es erlaubt, eine Fernsehkamera direkt mit dem Endoskop zu verbinden. Das Bild wurde übertragen auf Bildschirme im Operationssaal und auf verschiedene Abteilungen des Krankenhauses mittels einer geschlossenen Ringleitung. Dies erwies sich als von grossem Wert sowohl für den Unterricht als auch für die Konsultation.

# Bronchiectasis in the Aged*

JOHN B. ANDOSCA, M.D., F.C.C.P.**
Boston, Massachusetts

Autopsies performed at the Long Island Hospital on patients in the eighth, ninth, and tenth decades of life revealed a high incidence of bronchiectasis.

From 1943 to 1953 inclusive, out of a total of 254 autopsies in this age group, advanced bronchiectasis was discovered in 33 cases (13 per cent).

Bronchiectasis is a disease which is characterized by the pathological enlargement of one or more bronchi or bronchioles. The dilatation itself, however, is not the most important factor. The dilatation being only the demonstrable effect of a pathological process which damages the tissues of the bronchi and lungs sufficiently to interfere with their function.

Examination of the diseased bronchi reveals the loss of normal columnar ciliated epithelium. This is replaced in some cases by purely cicatricial tissue, and in others by stratified squamous cell epithelium. The basement membrane of the mucosa is likewise destroyed or damaged with disappearance of the elastic tissue fibers. The submucosa becomes densely fibrotic and rigid. In the vicinity of the lung parenchyma there appears to be laid down additional fibrosis which adds to the thickness and rigidity of the bronchial wall.

In addition to bronchiectasis, one usually finds varying degrees of pulmonary atelectasis, pneumonitis and fibrosis.

The maintenance of the self-cleansing mechanism of the tracheo-bronchial tree is of vital importance to an organ constantly exposed to foreign agents such as irritating dusts, particulate matter and bacteria. The factors concerned in protection of the respiratory tract are integrated by reflex activity so that gas exchange so necessary to survival is not impeded. The vibrissae serve as a gross filter and provide the first line of defense. The factors include ciliary activity, mucus formation, phagocytosis, cough and the peristaltic contraction of bronchial musculature.

Coughing represents a complicated reflex mechanism generally initiated by irritation of the nerve endings in the bronchial and tracheal epithelium. The forceful expiration of air carries the offending material out of the bronchial passages. With the diminished muscle tone, decreased sensitivity to stimuli and slowing of reflex activity so common in the ageing process, the inability to produce effective cough may result in inadequate elimination of bronchial secretions in elderly people and so predispose of pathologic states.

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*From the Long Island Hospital, Boston, Massachusetts.
**Formerly Medical Director, Long Island Hospital; Instructor in Medicine, Harvard Medical School and Physician in Division of Tuberculosis, Boston Health Department, Boston, Massachusetts.

It is important to note that there are certain conditions present in ageing which affect normal ciliary activity. These are excessive drying and atrophy of the epithelium, chronic infection, and the lack of integrity of the tissue fluids and electrolyte balance. When the ciliary system mechanism fails, secretions may accumulate in such large quantity that death from asphyxia is possible.

The inhaled swollen particles which are not conveyed up by ciliary activity or by the peristaltic movements of the swollen bronchi are absorbed by the wandering phagocytes and make their way into the circulation and lymphatics of the lung. Once ciliated epithelium is destroyed, it is not replaced. The rigidity of the walls of bronchiectatic bronchi precludes any possibility of bronchial peristalsis taking place. Atelectasis, pneumonitis or fibrosis of the surrounding *living* parenchyma, prevents admission of air which could play an important part in the expulsion of mucus, pus or foreign material from the damaged bronchi through the medium of coughing.

As would be expected, bronchiectasis is a progressive disease. In an involved lobe the retention of infection produces further destruction and damage to the tissue of the normal bronchi and living parenchyma. With increasing fibrosis and rigidity of the bronchial walls and lung parenchyma, drainage by means of coughing is further impaired, resulting in spread of the infection.

Age deteriorations may be present in almost all of the intricate mechanisms concerned in tracheo-bronchial elimination with resulting impairment of self-cleansing properties of the lung.

Aside from the occasional fusiform bronchial dilatation observed, the two distinctive types most commonly seen are cylindrical and saccular forms. Cylindrical bronchiectasis is the most common variety, and is found almost always in the base of the lung. The saccular type is found usually in the upper portion of the lung.

Bronchiectasis may be divided into four main types, depending upon the predominating pathology and location: (1) Fibrotic bronchiectasis is characterized by an abundance of peribronchial fibrosis. This type tends to favor progressive bronchial dilatation in the presence of infection. (2) Stenotic bronchiectasis favors development of atelectasis which, by virtue of its interference with bronchial drainage, favors spread of infection. (3) Ulcerative bronchiectasis produces varying degrees of hemorrhage from blood streaks to amounts endangering life. (4) The dry hemorrhage type of bronchiectasis is characterized by the absence of cough and sputum but by recurrent hemorrhages.

It has been noted that the majority of bronchiectatic lesions are traceable to any of the following pre-existing conditions such as recurring bronchial infection, lobar or lobular pneumonia, acute and chronic lung abscesses, sinusitis, asthma, bronchial obstruction due to carcinoma, foreign body, and inflammatory cicatrix in the bronchial lumen caused by specific infection such as tuberculosis. To a lesser extent, bronchiectasis may be the sequel of chronic empyema or lesions causing slow compression

of a bronchus, leading to retention of secretion with subsequent infection.

Clinical manifestations in bronchiectasis depend upon the degree of pathology present. Mild cases are characterized by slight cough, scanty amounts of sputum and rarely hemorrhage. Abnormal findings, when present, consist of diminished resonance and rhonchi over affected lobes. The diagnosis usually made at this stage is that of chronic bronchitis.

In far advanced stages bronchiectasis can be diagnosed readily. The clinical picture is apt to be severe. Cough may be constant. Sputum is abundant and may be foul. Varying degrees of dyspnea may be present. Finger clubbing is more frequent. Hemorrhage may be a serious problem.

It is, therefore, important to establish a diagnosis in the early phases of the disease so as to prevent late complications such as bronchopneumonia, atelectasis, empyema or marked hemorrhages. It has been noted that bronchopneumonia and bronchiectasis are frequent concomitants, the former occurring as a complication of the latter.

Roentgen findings in bronchiectasis vary considerably and diagnosis based upon plain films may be difficult. Yet the disease should be suspected when the following are present: (1) prominent bronchial markings, (2) rounded areas of increased radiance, (3) lobar or lobular atelectasis and (4) areas of mottled densities.

Although bronchography is an important and reliable procedure in the diagnosis of bronchiectasis, we do not advise it for elderly patients because of their limited pulmonary reserve. In addition, oil is usually retained in the chest of patients with asthma and emphysema. This may confuse subsequent roentgenograms and diminish the function of the involved alveoli. If the patient is a fit subject for surgical intervention, then bronchograms are definitely indicated in order to outline the normal and abnormal bronchi. Bronchoscopy may be of diagnostic value in differentiating foreign body, neoplasm or endobronchial tuberculosis.

Treatment of bronchiectasis in the aged should be directed in controlling intercurrent infections, removal of secretions, maintaining maximum vital capacity, a nutritious diet and chemotherapy.

Sex distribution of the 33 patients in this study was 28 males and five females. The great preponderance of male over female cases is undoubtedly due to the fact that in our chronic disease hospital we have twice

TABLE I
SEX AND AGE DISTRIBUTION

| | |
|---|---|
| Number of Autopsies | 254 |
| Bronchiectasis | 33 |
| Male | 28 |
| Female | 5 |
| Age Distribution—70 - 80 | 17 |
| 80 - 90 | 13 |
| 90 plus | 3 |

TABLE II
ETIOLOGIC FACTORS

| | |
|---|---|
| Pneumonia | 12 |
| Pleurisy | 6 |
| Tuberculosis | 6 |
| Bronchogenic Cancer | 4 |
| Asthma and Emphysema | 3 |
| Silicosis | 2 |

as many male as female patients. The youngest in the group was 70 years old and the oldest 91. See Table I.

Etiologic factors encountered in this series are tabulated in Table II. The high incidence of pneumonia and pleurisy is certainly striking. It was impossible to determine in most cases whether pneumonia caused the bronchiectasis or occurred because of bronchiectasis. Tuberculosis and bronchogenic carcinoma also were found to be important etiological factors.

TABLE III
MAJOR SYMPTOMS

| | |
|---|---|
| Cough | 31 |
| Sputum | 29 |
| Hemoptysis | 18 |
| Dyspnea | 15 |
| Chest Pain | 13 |

The chief symptoms of bronchiectasis were cough, sputum, hemoptysis, dyspnea, and chest pain. Table III shows the occurrence of these symptoms in the series under study. Almost all had cough with sputum.

It is important to note that over half the patients had hemoptysis at some time during the course of the disease. There is no doubt that practically all persons with bronchiectasis expectorate blood at some time. The amount may vary from tiny streaks to massive hemorrhage. Dyspnea and chest pain were also frequent symptoms.

Most of the patients had physical signs in the chest, although these were sometimes minimal, such as transient basal rhonchi, impaired resonance or slight suppression of breath sounds over the affected lobe. Clubbing of the fingers, long considered a classical sign of bronchiectasis,

TABLE IV
PHYSICAL SIGNS

| | |
|---|---|
| Positive Chest Findings | 29 |
| Clubbing of Fingers | 18 |
| No Physical Findings | 4 |

was present in 18. Its presence should always lead to consideration of the possibility of bronchiectasis but its absence obviously has no value in ruling out the disease. See Table IV.

Review of chest roentgenograms revealed that a high percentage were abnormal. Thirty of the 33 were abnormal in some respect and usually the proper diagnosis was at least suggestive. Bronchiectasis can be diagnosed accurately from such studies in most cases. Bronchograms may serve as a means of confirming the diagnosis and mapping out the diseased segments.

## *Case Reports*

*Case 1:* M. B., a 75 year old white male was admitted with a 10 year history of cough, expectoration of two or three ounces of yellowish-green blood streaked sputum and dyspnea on exertion.

Physical examination revealed coarse rales at both bases. There was marked clubbing of the fingers. In the past 10 years he had four attacks of pneumonia. He succumbed to his fifth attack (Fig. 1).

Autopsy revealed widespread bronchopneumonia, most marked in the lower lobes. There were numerous old and recent fibrotic adhesions. There was marked congestion and pulmonary edema. Bronchiectatic cavities in large numbers were present in both lower lobes. There was an old primary pulmonary complex in the lower lobe of the left lung and a calcified plaque at the apex of the right upper lobe.

*Case 2:* D. M., is an 86 year old white male, with a history of pulmonary tuberculosis for the past 20 years. His chief complaints were cough, expectoration of yellowish-green sputum, occasional bouts of hemoptysis and dyspnea. Physical examination revealed dullness and coarse rales over the left upper lobe and right base. Sputum was positive for tubercle bacilli. He succumbed to bronchopneumonia (Fig. 2).

Autopsy revealed advanced pulmonary tuberculosis of both upper lobes, especially the left in which area there were also a number of small cavities.

Marked bronchiectasis and bronchopneumonia were noted in both bases, particularly the right.

FIGURE 1

FIGURE 2

*Figure 1* (Case 1): Marked thickening and coarse infiltration of both bases, especially the right, with emphysema. *Figure 2* (Case 2): Thickened pleura over the left apex with coarse infiltration and multiple small cavities. Marked exaggeration of the right tracheo-bronchial tree with bilateral diaphragmatic adhesions. The heart and mediastinum is displaced to the left.

*Case 3:* W. W., a 74 year old white male, was admitted with a two months history of cough, sputum, chest pain and dyspnea. Physical examination revealed marked dullness over the lower half of the right lung. Fluid obtained from the right pleural cavity was bloody and was positive on Papanicolaou smear. He succumbed to bronchopneumonia (Fig. 3).

Autopsy revealed bronchogenic carcinoma involving the right main bronchus 3 cm. from its origin. In the right lung below the obstructed main bronchus, there was marked bronchiectasis and atelectasis. Both lungs showed confluent bronchopneumonia.

*Case 4:* J. D., an 82 year old white male, was admitted with a 10 year history of cough, sputum, occasional streaking, weakness and dyspnea on exertion. For the past 20 years, he had complained of asthma and chronic bronchitis. Physical examination revealed impaired resonance and coarse rales at both bases. There was marked clubbing of the fingers. He succumbed to bronchopneumonia (Fig. 4).

Autopsy revealed bilateral confluent bronchopneumonia. Advanced bronchiectasis was noted in both lower lobes, extending into the periphery of the lungs. In addition, the right middle lobe showed moderate fibrosis of the parenchyma.

## CONCLUSIONS

Bronchiectasis in the aged is a common disease.

Autopsy findings on 254 patients, ranging from 70 to 91 years, revealed bronchiectasis in 33 (13 per cent).

Bronchial obstruction and infection are two of the most important causes of bronchiectasis.

In this series, the most common etiologic factors encountered were pneumonia, pleurisy, tuberculosis and bronchogenic carcinoma.

Symptoms were usually cough, sputum, hemoptysis and dyspnea. Physical findings in the chest and clubbing of the fingers were present in almost all of our cases.

Bronchiectasis can be diagnosed accurately in most cases by plain roentgenograms.

FIGURE 3

FIGURE 4

*Figure 3* (Case 3): Marked density involving the lower half of the right lung, having the appearance of consolidation or fluid. Coarse infiltration extending out from hilar regions. *Figure 4* (Case 4): Thickened pleura and a calcified area at the right apex with small calcified nodes in both lungs. Thickening and coarse infiltration at both bases.

Instillation of iodized oil in this age group is contraindicated.

The treatment of bronchiectasis in the aged should be directed in controlling intercurrent infections, removal of secretions, nutritious diet and chemotherapy.

## CONCLUSIONES

La bronquiectasia en los ancianos es una enfermedad común.

Los hallazgos de autopsia en 254 enfermos entre 70 y 91 años, revelaron bronquiectasia en 33 (13 por ciento).

La obstrucción bronquial y la infección, son dos de las causas más importantes de bronquiectasia.

En esta serie la etiología mas común fué: neumonía, pleuresía, tuberculosis y carcinoma bronquiogénico.

Los síntomas habituales son: tos, esputos, hemoptisis y disnea.

Los hallazgos físicos en el tórax y lo dedos hiprocráticos, se encontraron en casi todos los casos nuestros.

La bronquiectasia puede diagnosticarse exactamente en la mayoría de los casos por la radiografía simple.

La instilación de aceite yodado en el grupo de esta edad está contraindicada.

El tratamiento de la bronquiectasia en los ancianos debe dirigirse hacia el control de las infecciones intercurrentes, expulsión de las secreciones, dieta y quimioterapia.

## RESUME

La bronchiectasie est une affection fréquente chez les individus âgés.

Les constatations d'autopsie chez 254 malades, allant de 70 à 91 ans, révélèrent l'existence de bronchiectasie chez 33 d'entre eux (13%).

L'obstruction bronchique et l'infection sont deux des causes les plus importantes des dilatations bronchiques.

Dans cette série de cas, les facteurs étiologiques le plus souvent rencontrés furent la pneumonie, la pleurésie, la tuberculose et le cancer bronchique.

Les symptômes furent habituellement la toux, l'expectoration, l'hémoptysie, et la dyspnée. Des signes physiques à l'examen thoracique, et l'hippocratisme digital furent observés dans presque tous les cas.

La dilatation bronchique peut être diagnostiquée d'une façon courante par de simples radiographies dans la plupart des cas.

L'instillation d'huile iodées est contrindiquée dans ce groupe de malades âgés.

Le traitement de la bronchiectasie chez les personnes âgées devrait viser à juguler les infections intercurrentes, calmer les sécrétions et comprendre un régime nutritif et la chimiothérapie.

## SCHLUSSFOLGERUNGEN

Die Bronchiektasie bei betagten Menschen ist eine häufige Krankheit. Sektionsbefunde bei 254 Kranken im Alter zwischen 70 und 91 Jahren erbrachten eine Bronchiektasie dei 33 Fällen = 13%. Ein Bronchialver-

schluss und eine Infektion sind 2 der wichtigsten Ursachen für Bronchiektasie.

In dieser Untersuchungsreihe waren die am häufigsten auftretenden aetiologischen Faktoren Pneumonie, Pleuritis, Tuberkulose und Bronchialcarcinom. Die Symptome bestanden für gewöhnlich in Husten, Auswurf, Haemoptysen und Dyspnoe. Physikalische Thoraxbefunde und Trommelschlägelfinger lagen in fast allen unseren Fällen vor. Die Bronchiektasie kann in den meisten Fällen richtig diagnostiziert werden durch klare Röntgenübersichtsaufnahmen. Die Einführung von Jodöl bei dieser Altersgruppe ist kontraindiziert. Die Behandlung der Bronchiektasie im höheren Alter muss sich auf die Bekämpfung interkurrenter Infektionen richten, auf die Entfernung von Sekreten, eine nahrhafte Kost und Chemo-Therapie.

# Case Report:

# Diffuse Interstitial Pulmonary Fibrosis (Hamman-Rich Syndrome): Diagnosis by Lung Biopsy; Treated with Cortico-Steroids*

ELLIS J. VAN SLYCK, M.D., F.C.C.P.
Detroit, Michigan

From reports of diffuse interstitial fibrosis of the lungs which have sporadically appeared in the American literature in the last eight years,[2-16] it is apparent that the original term "acute" applied to this disease by Hamman and Rich[1] in their original description of four cases, no longer pertains to many of the cases. Furthermore, it would seem that the number of authentic cases now known is too meager (about thirty) to draw any satisfactory conclusions regarding etiology, response to treatment, and clinical course, for, as the case herein reported demonstrates, remarkable remissions are apparently possible. The following case is reported because it is that of a living patient whose diagnosis was established fairly early in the course of her illness, and because of surprising response to steroid therapy.

*Case 1:* G. A. A 51 year old white widow entered the hospital on September 30, 1954 with a six month history of progressive dyspnea, hard cough occasionally productive of tenacious, ropy sputum, associated with anorexia and a 25 pound weight loss. Symptoms evolved gradually from a severe chest cold which she contracted seven months previously. She denied chills, sweats, or hemoptysis. There was also an absence of ankle edema, and she got the greatest relief of dyspnea by lying supine. She continued to work as a waitress until the progression of cough and dyspnea compelled her to seek medical care. Her past medical history was devoid of significant events, and there was no known exposure to noxious vapors or dusts.

Physical examination revealed a dyspneic, cyanotic, chronically ill middle-aged white female. She weighed 160 pounds. The temperature and pulse rate were normal. The blood pressure was 110/80 mm. of mercury. The respirations were slightly rapid and labored. Prominent clubbing of finger and toenails was apparent. Other significant physical findings were: An increased anterior-posterior diameter of the thorax, showers of dry, crepitant rales over both lungs from apex to base at the end of inspiration. The second sound over the pulmonic area was louder than the aortic second sound, but otherwise the heart findings were normal. Pertinent by their absence were the lack of venous distention, edema, abdominal splanchnomegaly or lymphadenopathy.

*Laboratory Data:* hemoglobin 13.8 grams per cent; white blood cell count 15,150 per cubic millimeter. Differential leukocytic count 66 per cent polymorphonuclear leukocytes, 28 per cent lymphocytes, 3 per cent monocytes, and 3 per cent eosinophils. Total serum protein was 7.7 grams per cent with a normal albumin/globulin ratio. Serum amylase was 118 units (normal 80-180 units). Duodenal drainage studies were normal. The urine showed a faint trace of albumin but was otherwise normal. Examination of stool for blood and parasites was negative. Sputum cultures revealed no significant organisms including those for tubercle bacilli. Sputum smears showed only a rare eosinophil. Histoplasmin and tuberculin skin

*From the Department of Medicine, The Alexander Blain Hospital and Clinic.

FIGURE 1

FIGURE 2

FIGURE 3

*Figure 1:* Posterior-anterior film of chest taken on September 30, 1954. There is a diffuse mottled and linear increase in pulmonary markings.—*Figure 2:* Posterior-anterior film of chest taken on October 11, 1955. A definite increase in cardiac size, apparently left ventricular, is now evident.—*Figure 3:* Posterior-anterior film of chest taken on August 31, 1956. Although patient at this time is clinically much improved, there is little change in appearance of pulmonary parenchyma.

tests were negative. X-ray of the chest revealed a universal mottled increase in pulmonary markings without pleural effusion, and apparent left ventricular enlargement (Figure 1). Electrocardiogram was normal (Figure 4).

*Subsequent Course:* The patient left the hospital after two weeks' treatment with bronchodilators, sputum liquifiers, and digitalization, although there had been no improvement in the appearance of the chest film. A relapse necessitated readmission on November 14, 1954. A scalene node biopsy done on November 18, 1954, showed only nonspecific chronic lymphadenitis. Cell block study of sputum was negative for malignant cells. A lung biopsy was performed through the right second intercostal space anteriorly on November 30, 1954 (Figure 6).

FIG. 4

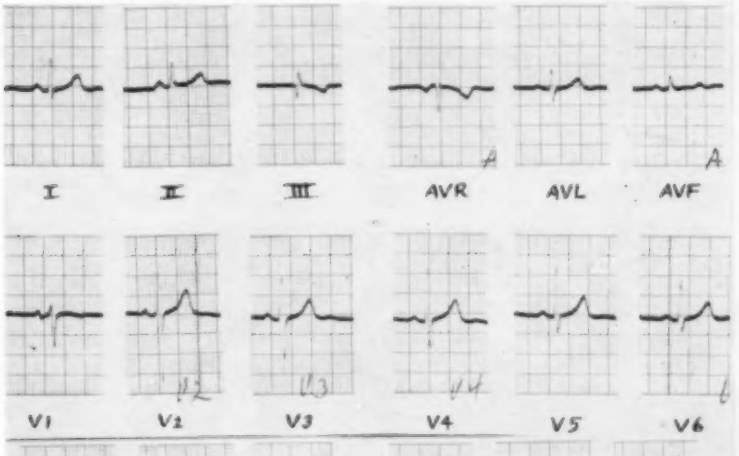


FIG. 5

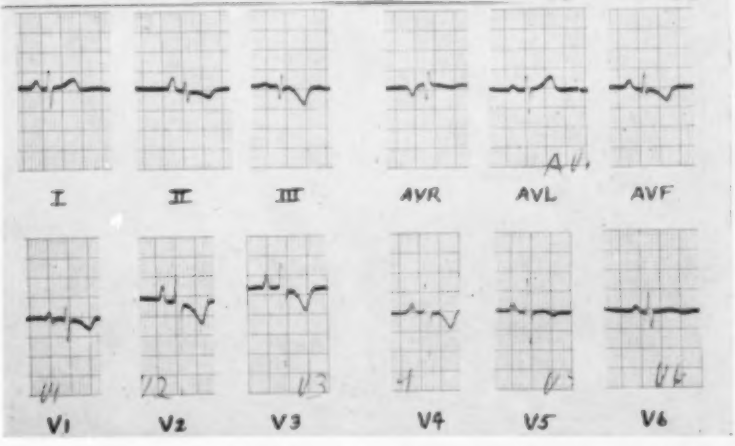


*Figure 4:* Electrocardiogram obtained on November 15, 1954 interpreted as being within normal limits.—*Figure 5:* Electrocardiogram obtained on October 10, 1955, showing the appearance of right ventricular hypertrophy since the previous tracing.

*Microscopic Description of Lung Biopsy:* All of the segments of lung biopsy tissue are essentially similar. They consist of fairly uniform and diffuse alveolar septal thickening. Alveolar lumina are empty, except for scattered clumps of fresh erythrocytes interpreted as the artifacts of operative trauma. While the alveolar septal thickening is partly fibrous, high power examination reveals considerable capillary engorgement and apparent duplication resulting in from two to four capillaries within such a thickened septal wall. Under the phase microscope, delicate fibers, presumably reticulum surround the proliferated capillaries. These findings are in agreement with those previously seen and described by Golden and Bronk.[13] The tissue pattern of diffuse, interstitial fibrosis conforms, in essential details, to that described by Hamman and Rich.[1]

Over the next four months the patient received three courses of nitrogen mustard (26 milligrams, 26 milligrams, and 24 milligrams respectively) with no effect on her condition. There was a progressive hemoglobin rise during this therapy from 14.4 grams per cent to 18.9 grams per cent. At all times during this period her condition was considered critical because of the intense dyspnea. She was followed as an outpatient from April to October 1955 when the appearance of right-sided heart failure made rehospitalization necessary. Further enlargement of the heart was now present (Figure 2) as was a clear-cut electrocardiographic picture of

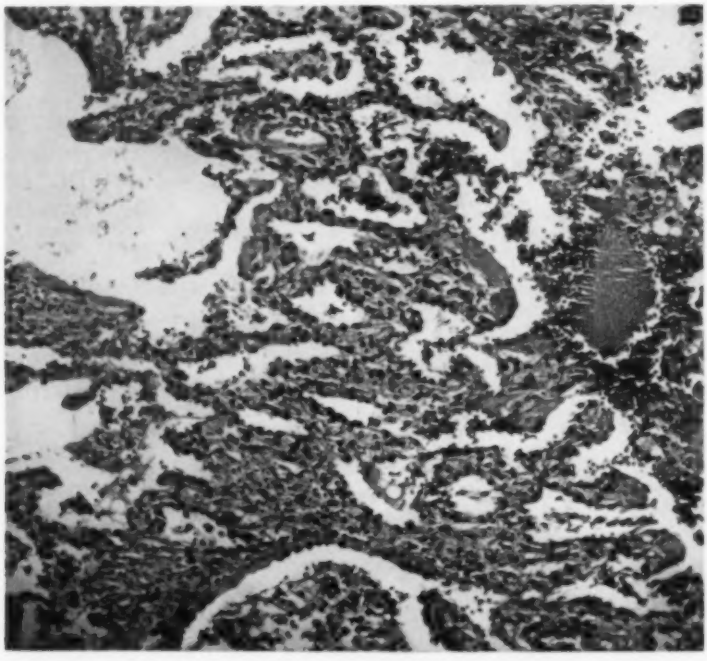

FIGURE 6: Diffuse alveolar septal thickening results in three to five fold increases in thicknesses. Alveolar lumina are, for the most part, empty except for clumps of red blood cells, interpreted as operative artifacts.

right ventricular hypertrophy (Figure 5) and polycythemia. Treatment with oxygen, diuretics, digitalis, and venesection resulted in clinical improvement, and a weight loss from 122 pounds on admission to 105 pounds on discharge, October 28, 1955.

A massive epistaxis with a precipitous fall in hemoglobin from 16.8 grams per cent to 5.6 gram per cent, with attendant air hunger, shock, and left ventricular failure caused her last admission on December 30, 1955. She responded somewhat to oxygen and blood replacement, but because her condition seemed critical she was given corticotropin; (40 units in 16 per cent gelatin daily) and subsequently switched to prednisone. Within 48 hours of starting this therapy there was a dramatic improvement in dyspnea and appetite. Four days later she was able to be out of oxygen permanently. She continued to improve until subjectively and objectively she was better than at any time in almost three years. She left the hospital on January 25, 1956 and has been followed regularly as an outpatient up to the time of writing in October, 1956. She has continued to maintain her improvement. She is now taking 10 milligrams of prednisone daily, and has experienced no unpleasant side-effects. Her weight is steady at 135 pounds without evidence of congestive failure. Although the cyanosis has virtually disappeared, the clubbing has not appreciably receded. The dry, fine rales on terminal inspiration, which has been a constant characteristic of her disease, remains, and the second pulmonic heart sound is still extraordinarily loud. A recent electrocardiogram shows less obvious evidence for right ventricular hypertrophy than previously, although this may be the result of super-imposed left ventricular hypertrophy. A recent chest x-ray shows no essential change in heart or lungs (Figure 3). Hemoglobin at present is 16.4 grams per cent. She has returned to her job as a waitress in the past month.

## *Discussion*

Prior to this case there have been only five instances in which an antemortem diagnosis of the Hamman-Rich Syndrome has been reported.[5-9] Lung biopsy was the crucial procedure in each case—as it was here. Several other cases have been suspected during life on clinical grounds without microscopic corroboration.[5-8, 10, 13-15]

With the exception of the case reported by Pinney and Harris,[9] treatment of any kind has been uniformly unsuccessful. Particularly have there been reports of harmful effects on the course of the disease by cortico-steroid therapy. Those few cases have been well-summarized by Clough.[16] Briefly, cases treated early in their course with steroids may show temporary improvement, but this is followed by rapid fatal exacerbations upon reducing the dose below a critical level. Other cases treated late in their course have had either no ameliorative response or an apparent increase in the rapidity of their downhill trend.

Pinney and Harris[9] reported a case in 1956 in which diagnosis was established early by lung biopsy, and subsequent treatment with corticosteroids resulted in a remarkable remission of signs and symptoms which

persisted 17 months (at which time the case was reported). The daily maintenance dose of cortisone was 40 milligrams. Our case parallels the one of Pinney and Harris closely in many respects. Although our patient's chest film has shown little or no change, and there are still signs of pulmonary disease present, the clinical improvement is comparable to their case. The maintenance dose, 10 milligrams of prednisone, in our case corresponds to 40 milligrams of cortisone used to maintain theirs.

It would seem that our case can be added to that of Pinney and Harris to cast some doubt on the validity of the conclusion reached by previous authors—namely that cortico-steroids are contraindicated in treating known or suspected cases of the Hamman-Rich syndrome, and points up the fact that no hard and fast deductions can be drawn from such meager clinical material as we have at present. The use of lung biopsy early in patients who defy accurate diagnosis by the usual means may result in more cases of the Hamman-Rich syndrome being brought to light, and their subsequent course more intelligently observed.

*Acknowledgment:* The interpretation and description of the microscopic pathology was contributed by Dr. Alfred Golden, and is gratefully acknowledged.

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# Editorial

## The Treatment of Congestive Heart Failure

The treatment of congestive heart failure is based upon the four "D's".

A. *Decubitus*

1. Decubitus means the position of the patient at rest. Heart patients should remain at rest in the position that best gives them the most comfort.

2. They remain at rest until compensation is restored and they are then permitted to go on graduated exercise.

3. A commode is used rather than a bedpan.

Graduated activity serves two purposes: (1) It informs the physician of the patient's limitations by virtue of his heart disease, and (2) it enables him to regain muscle tone and well being following confinement. The only physical limitation to be placed upon the patient on returning to activity is that placed on him by his cardiac reserve and not iatrogenically.

B. *Diet*

The patient is placed on a 400 milligram low sodium diet with fluids restricted to 2,000 cc. daily. If he is obese the diet is reduced to 1200 calories. The diet is supplemented by multi-vitamins and he remains on the diet as long as it is indicated.

C. *Drugs*

1. *Acidifying agents.* If not contraindicated 90 grains of ammonium daily are given four days during the week. Once diuresis has occurred the ammonium chloride may be discontinued or a "maintenance" dose of 45 grains a day, four days a week, may be continued.

2. *Aminophyllin. Aminophyllin* is only used intravenously in doses of 3¾ or 7½ grains for the relief of pulmonary edema and dyspnea.

3. *Anticoagulants.* Heparin is used for rapid action. The dose is 50 milligrams in sterile water intravenously every four hours. This is continued as often as necessary to keep the coagulation time between 30 and 40 minutes. At the time heparin is started dicumarol is also begun, the dose being 300 milligrams the first day, 200 milligrams the second day, and 100 milligrams daily on the third day. The dose of dicumarol is then empirically determined in order to keep the prothrombin time between 20 and 30 per cent of normal. The coagulation time and prothrombin time are both determined before the anticoagulants are instituted. The tests are repeated daily. The heparin and coagulation time may be discontinued as soon as dicumarol activity has reached its maximum effect. The length of time to continue the anticoagulants is controversial and varies with each observer.

4. *Cathartics.* Cathartics must be administered in sufficient strength to avoid constipation and also to avoid straining and cramping at the stool.

5. *Digitalis.* The whole leaf preparation digitora is used in 1½ grain tablet. It is given orally one tablet four times a day until digitalization has occurred and then one tablet daily thereafter for a maintenance dose. Digi-

toxin 1.2 milligrams may be given as the total digitalizing dose orally in emergencies. However, if no emergency exists 0.2 milligram tablet is given every half hour until the patient is digitalized. The maintenance dose is 0.1 to 0.2 mg. daily.

Cedilanid is used intravenously and the digitalizing dose is 8 cc. which may be given totally in an emergency. If no emergency exists the drug may be administered in dosage of 4 cc. at onset and then 2 cc. every hour until the digitalization has occurred.

Warnings concerning digitalis

1. Don't digitalize a patient rapidly if he has been on digitalis.
2. Don't digitalize the elderly or aged rapidly.
3. Don't digitalize rapidly a patient with a recent myocardial infarct.
4. Don't give the first doses of a mercurial diuretic just after completing digitalization.
5. Don't use intravenous calcium salts with digitalis.

6. *Glucose.* May be used intravenously if it is indicated.

7. *Opiates.* Morphine grains ¼ with atrophine sulphate grains 1/150 is recommended as often as necessary. If the patient has an idiosyncrasy to the drug some other opiate may be substituted.

8. *Oxygen.* May be used whenever indicated.

9. *Sedatives.* Sedatives and tranquilizing agents are important in the treatment of congestive heart failure.

D. *Diuretics*

1. At the start of treatment 1 cc. of salyrgan-theophyllin is given daily intramuscularly until maximum diuresis is established and the weight becomes constant.

2. The diuretic is then continued at regular intervals which have been determined empirically for the individual patient. The mechanical removal of the fluid may be necessary. Southey tubes may occasionally be used with antibiotics as an adjunct to prevent infection.

The treatment of congestive heart failure is time consuming and requires infinite attention to detail. The basis for the treatment of congestive heart failure depends on (1) proper decubation -and- proper ambulation; (2) special diets as long as they are indicated; (3) drugs, particularly digitalis, used in full digitalizing doses continuing with the maintenance dose of the drug; and (4) the intelligent use of diuretics both therapeutically and prophylactically.

JOHN F. BRIGGS, M.D., F.C.C.P.

# Teaching Chest Disease
# Diseases of the Chest in a New Curriculum

HARVEY J. MENDELSOHN, M.D., F.C.C.P.*
Cleveland, Ohio

Basic objectives of good medical education have changed little in the past 50 years. The tremendous advances in the preclinical sciences and in clinical medicine during this time have made it impossible for a faculty to impart this mass of knowledge or, indeed, to expect or require the student to know all of it. This became more apparent with the accelerated program required for undergraduate medical education during World War II. It was also felt that the social and economic changes that have occurred deserved more recognition.

Therefore, in 1946, the faculty of the School of Medicine of Western Reserve University, under the leadership of its Dean, Dr. Joseph T. Wearn, began to plan a new curriculum approaching it as a scientific experiment. In 1952, the new curriculum was implemented, and in 1956, the first class under the new curriculum was graduated. I have drawn largely from the reports of Wearn,[1] Ham,[2] Patterson,[3] and Caughey,[4] and my own experience as a participating faculty member.

The objectives of this curriculum are to graduate a physician with adequate knowledge and skills, who has proper professional ideals and scientific attitudes. Since knowledge is not static, a strong effort is made to develop habits of self-education which, it is hoped, will continue throughout life. It was realized that the example set by the faculty would play an important role.

The idea of total coverage was abandoned from the outset. It was agreed to emphasize basic concepts and their application to the mechanisms of disease. To do this better, the previously existing more or less sharp separation of teaching along purely departmental lines was altered so that from the first day of medical school, teaching would be on an interdepartmental basis. Therefore, the material has been organized into subject groupings. Each subject is taught by a subject committee made up of members from the departments concerned. It was also felt that the introduction of the student to the patient should be early in the first year rather than at the end of his second year. The course in clinical science, described below, is designed to do this.

The usual four year curriculum has been divided into three phases. Phase 1, occupying the first year, is concerned with normal structure and function. Phase 2, in the second year and first half of the third year, studies disorders of structure and function. Phase 3, during the last year and one-

*Assistant Professor of Thoracic Surgery, Department of Surgery, Western Reserve University School of Medicine, and University Hospitals.

The first in a new series of articles prepared under the sponsorship of the Council on Undergraduate Education of the American College of Chest Physicians.

half, includes the required and elective clerkships and study of non-hospitalized patients. Basic science is brought into Phase 3 with bioclinical seminars.

The introduction to the patient is started early in Phase 1 under the course in clinical science. Each student is assigned to a woman in the prenatal clinic and follows her through to delivery. He then follows the mother and child in a family clinic through Phases 1 and 2. He observes how medical care is administered and meets twice weekly in a small group with a clinical preceptor to discuss the various inter-relationships and problems. Here, interviewing technics and the technics of physical examination are taught and practiced in relation to the gross anatomy of the various systems as studied. Lectures are given weekly on these technics, the family relationship, and growth and development of the infant. The curriculum is outlined in Table I.

The way in which a subject committee operates can be illustrated by the organization of the respiratory committee in Phase 1 and 2. In Phase 1, the respiratory and cardiovascular committees are combined. The chair-

TABLE I

| | | |
|---|---|---|
| Phase 1 | (two semesters): Normal Structure and Function | |
| | Cellular biology | |
| | Tissue biology and the neuromuscular system | |
| | Cardiovascular and respiratory system | |
| | Metabolism (gastrointestinal tract, liver, kidneys) | |
| | Endocrine and reproductive systems | |
| | Clinical science | |
| Phase 2 | (three semesters): Disorder of Structure and Function | |
| | Introduction to disease | |
| | Chemical agents | |
| | Infectious diseases | |
| | Cardiovascular system | |
| | Respiratory system | |
| | Hematopoietic system | |
| | Gastrointestinal system | |
| | Genitourinary system | |
| | Skin | |
| | Nervous system | |
| | The special sense organs | |
| | Locomotor system | |
| | Metabolism and the endocrine system | |
| | Organs of reproduction | |
| | Clinical science | |
| Phase 3 | (three semesters): The Care of the Patient | |
| | Basic clerkship | 4 mo. |
| | Obstetrics and gynecology | 2 mo. |
| | Group clinic | 2 mo. |
| | Surgery | 2 mo. |
| | Elective clerkships | 6 mo. |
| | Continuity program | ¾ day/wk. |
| | Basic science | ½ day/wk. |

man and co-chairman are from the Department of Physiology. There are two representatives from the Department of Anatomy and one each from the Departments of Biochemistry and Medicine. The committee decides what the course will cover, what lectures will be given, who will give them and what experiments will be done. A period of seven weeks is allotted with two and one-half full days of classes and laboratory exercises each week. The majority of the time is devoted to gross and microscopic anatomy, physiology and biochemistry. Three clinics are given by the representative from the Department of Medicine. These are not to teach disease processes but to show how alterations of physiological and biochemical processes are produced by diseases such as emphysema, asthma, pleural fibrosis or effusion. During this period the principles involved in the physical examination of the chest are taught in the clinical science course. This is correlated with the teaching of anatomy of the thorax and its contents both gross and microscopic.

In Phase 2, the respiratory disease committee is now headed by a pathologist with two representatives from the Departments of Medicine and Surgery, and one each from the Departments of Preventive Medicine and Microbiology. A total of 20 additional faculty members participate in the teaching effort. They come from the Departments of Pathology, Microbiology, Psychiatry, Radiology, Medicine, Surgery and Preventive Medicine.

Three consecutive weeks with three and one-half days each have been allotted for the teaching of this subject. This adds up to 74 hours of laboratory exercises, lectures and clinics. Fourteen hours of this time are used for the teaching of diseases of the ear, nose and throat. The remaining 60 hours are used as outlined in Table II.

It can be seen that lectures, clinics and laboratories do not attempt complete coverage. A syllabus is provided with outlines of the material presented and appropriate references to texts and original articles from the literature. Explanatory diagrams and additional notes are included in the syllabus as deemed necessary by the responsible faculty member. The reference material is made available in the library as each subject is presented.

TABLE II

| | |
|---|---|
| I. | *Pathology Lectures* (six hours)—Pulmonary Tuberculosis, Mycoses, Pneumoconioses, Tumors of the Thorax, Disease of the Pleura and Microbiology of the Respiratory Tract. |
| II. | *Clinical Lectures* (four hours)—Acute Respiratory Diseases, Respiratory Physiology and Pulmonary Function, Asthma and Emphysema, the Physiology of Cough. |
| III. | *Clinics* (10 hours)—Bronchogenic Carcinoma, Pulmonary Vascular Diseases, Pneumoconioses, Chest Trauma, Pulmonary Fibrosis, Bronchial Obstruction, Combined Tuberculosis Therapy Conference (two hours), Clinical Pathological Conference (two hours). |
| IV. | *Laboratory Exercise* (40 hours)—X-ray Conference (three hours), Pulmonary Function Methods (three hours), Microbiology of the Respiratory Tract (four hours), Anatomy, Microscopic and Gross Pathology (20 hours). |

The student is encouraged and expected to use the references to extend his knowledge.

The advantages of the subject committee method are many. It increases the all too infrequent contact of faculty members with each other on a professional basis. It brings agreement on what should be taught and who should teach it. It prevents unnecessary repetition and confusion of the student by contradictory opinion. From the standpoint of the student, the learning process is faciliated by correlating the various basic sciences with each other and with clinical science in the same period of time.

From the standpoint of teaching diseases of the chest, it is felt that a better basic concept of the problems and methods of diagnosis are obtained. The question of coverage is still being raised, and it is realized that an acceptable balance may be hard to obtain. At present the students use the bibliography given in the syllabus. The results of the final examinations indicate that approximately half of the class cover the field well in their reading.

There is not sufficient space to discuss the alterations of the clerkships that have taken place in Phase 3. Suffice it to say that the student seems to have learned as much under this system as under the old system. However, his exposure to patients with "medical" and "surgical" chest disease problems is dependent upon the patients he happens to see during his four-month basic clerkship unless he takes an elective clerkship in diseases of the chest or medicine or thoracic surgery. This will be partly remedied now that a required two-month surgical clerkship has been added which will include some thoracic surgery. We feel he understands basic concepts better and should be better able to investigate a patient on his own.

In conclusion, it should be remembered that this curriculum is not fixed. Changes are being made and will continue to be made to improve the quality of teaching.

It is my impression that this correlated method of teaching has given our students a clear total picture of the pathology, pathogenesis and basic physiological mechanisms involved in the disease processes of the chest (and other systems). This was not usually well correlated in the classical organization of the curriculum. Our students have done as well or better than their predecessors in application of these principles to the diagnosis of diseases of the chest. The sacrifice of a formal total coverage was inevitable and is no great loss. The normal drive of each student to learn has been sufficient to make him adequately "cover" each subject by further reading on his own.

## REFERENCES

1 Wearn, J. T.: "Reports on Experiments in Medical Education-Background and Philosophy of Experiment," *Jour. Med. Education*, 31:516, 1956.

2 Ham, T. H.: "Reports on Experiments in Medical Education—Methods in Development and Revision of a Program of Medical Education," *Jour. Med. Education*, 31: 519, 1956.

3 Patterson, J. W.: "Reports on Experiments in Medical Education—Interdepartmental Teaching of Medicine and Biologic Science in Four Years," *Jour. Med. Education*, 31:521, 1956.

4 Caughey, J. L., Jr.: "Reports on Experiments in Medical Education—Clinical Teaching During Four Years," *Jour. Med. Education*, 31:530, 1956.

# The President's Page

It gives me great pleasure to invite all the members of the College to the annual meeting in New York the last of this month. An excellent program has been arranged by the Committee on Scientific Program, under the chairmanship of Dr. Pfuetze. I am confident that all of you will enjoy the program and draw much that is valuable from it. New York is an appropriate locale for our meeting, because it affords splendid meeting and hotel facilities. Moreover, it is a city that cannot fail to be attractive to your wife while you are attending meetings, for Manhattan has something to capture the interest of every woman. By all means have your wife accompany you on this trip.

The wisdom of attending the various scientific programs that have been arranged must be evident. Much can be learned, too, by inspection of the many interesting exhibits. No less important to all of us is your participation in the administrative activities of the College. In these times of accelerated change, the College and medicine in general urgently need your assistance and counsel. It is only by means of constant vigilance and the cohesive power of cooperative effort that we can fulfill our responsibility to society as the guardians of public health. We must constantly be alert to ward off the insidious activities of the unscrupulous and the mercenary who seek to prey upon the public. You can do much to defend, preserve and improve our system of medicine by active participation in the activities of the College. Make full use of the various committees that have been established to deal with specific problems, and do not hesitate to make your thoughts and opinions known. Although a single voice may not always be heard, it may have far-reaching effects when it is augmented by others.

This is my last letter addressed to all the members of the American College of Chest Physicians as your president. I wish to thank all of you for the honor you have conferred upon me. You have cooperated to the utmost when called upon, and your advice and assistance have been deeply appreciated and, I hope, have been requited in some measure. Although many of the objectives we set for ourselves have not been attained, I think we may allow that some progress has been made. Our membership has continued to increase, not only in number but also in eminence, and every man has reason for pride at being included in it.

May I express my gratitude to my fellow officers of the College, to the many members of the various committees, and to members of the staff of the Executive Office, for their unsparing support and help. As your presiding officer, one of the most gratifying experiences to me has been the uncommon opportunity to make new friends as well as to enhance friendships long established. Mrs. Moersch and I reiterate our indebtedness to you all for your many kindnesses to us during the past year. We hope we can greet and thank you personally at the meeting in New York.

A. J. Moersch

## 23RD ANNUAL MEETING OF THE COLLEGE

You will not want to miss the interesting papers and popular features arranged by the Committee on Scientific Program for the 23rd Annual Meeting of the American College of Chest Physicians. In addition to the regular scientific sessions, your committee has arranged the following special sessions:

| | |
|---|---|
| Seminars | X-ray Conference |
| Round Table Luncheons | EKG Conference |
| Fireside Conferences | Motion Picture Program |
| Panel Discussions | Annual College Conference |

Open Forum sponsored by the Council on Hospitals
Teaching Seminar sponsored by the Council on Undergraduate Medical Education
Social activities and special program for the ladies

Prominent speakers will take part in all of these sessions. Please see the program published in the March issue of *Diseases of the Chest* for detailed information, or write to the Executive Offices of the College, 112 East Chestnut Street, Chicago 11, Illinois, for a copy of the program.

## IMPORTANT!

### Advance Registration for College Annual Meeting

Advance registration has been established for the convenience of College members who will be attending the Annual Meeting in New York City in order that they may avoid waiting in line at the registration desk. Each member who has returned an advance registration form will have his badge prepared at the Executive Offices of the College and checked for correct spelling. The badge, tickets, program, and other essential information will be delivered to him in one package at the Registration Desk with the least amount of inconvenience. We encourage every member of the College to take advantage of the advance registration procedure and to make early hotel reservations. For accommodations at the Hotel Commodore, please write directly to the hotel, New York City 17, giving arrival and departure dates or complete the reservation form appearing on p. xx of this issue. Please be sure to indicate that you will attend the meeting of the American College of Chest Physicians.

Tickets for the Seminars and Round Table Luncheons are limited and places are assigned on a first-come, first-serve basis. Members ordering tickets for these sessions in advance are more likely to be able to attend those of their choice, as many of them are completely sold out prior to the meeting.

Please complete the coupon in the March issue of *Diseases of the Chest*, or in the program mailed to members. Additional copies of the program containing advance registration forms, will be sent upon request. Please write to the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

## ANNOUNCEMENT

The L. Frank Burris Resident Fellowship Fund has been established through the generosity of his daughter, Mrs. A. M. Burris LaCorte, Stanford, Connecticut. Mr. Burris of the Lazy E Ranch, Silver City, New Mexico and El Paso, Texas, passed away on March 19, 1957. Mrs. LaCorte is the wife of Dr. Salvatore LaCorte, a member of the American College of Chest Physicians.

## FELLOWS VISIT COLLEGE CHAPTERS

**Dr. Harold G. Trimble,** Oakland, California, Regent of the College, and **Dr. Emil Bogen,** Olive View, California, lectured before many of our College chapters on recent trips. Dr. Bogen, on a world tour, visited our chapters in Europe and the Middle East, arriving in India at the time of Dr. Trimble's trip to the Far East.

### Italian Chapter

On November 19, 1956, Dr. Bogen presented a paper on "Epidemiology of Tuberculosis" before a special meeting of the Italian Chapter of the College held at the Forlanini Institute in Rome. At a second meeting, he spoke on "Mortality Rates in Tuberculosis." Both of these meetings, arranged by Prof. Dr. A. Omodei Zorini, Regent of the College for Italy, were attended by many College members and other physicians in Rome. Following Dr. Bogen's lectures, he was guest of honor at a dinner given by Prof. Zorini.

Left to right: Dr. Emil Bogen, Prof. A. Omodei Zorini, Prof. Giusto Fegiz, Rome, Italy.

### Greek Chapter

In Athens, on November 21, 1956, Dr. Bogen lectured on "The Epidemiology of Tuberculosis" at a joint meeting of the Tuberculosis and Surgical Societies at the University of Athens. On November 22, he presented a second lecture on "The Bacteriology of Tuberculosis" at the Sotiria Sanatorium before the Greek Chapter of the College and the sanatorium staff. This meeting was followed by a dinner given in his honor by members of the Greek Chapter. Dr. Panayiotis Chortis, Governor of the College for Greece, made arrangements for the two meetings which were well attended.

### Turkey

During Dr. Bogen's visit in Istanbul on November 28, a special meeting of College members was held, at which time plans were made for the formal organization of the Turkish Chapter. Immediately after the business session, Dr. Bogen spoke on "The Epidemiology of Tuberculosis." Following his lecture, Dr. Bogen attended a dinner given by the Turkish members at the Divan Hotel. Prof. Dr. Tevfik Saglam of Istanbul, Regent of the College for Turkey, arranged for the organizational meeting and for Dr. Bogen's lecture.

The formal organization of the Turkish Chapter took place in Istanbul during the 3rd Turkish National Tuberculosis Conference, on January 19, 1957, and the following officers were elected:

| | |
|---|---|
| President: | Tevfik Saglam, Istanbul |
| Vice-President: | Ihsan Rifat Sabar, Istanbul |
| Secretary-Treasurer: | Celal Ertug, Ankara |

Dr. Emil Bogen lecturing in Istanbul. To the right, Prof. Tevfik Saglam, Regent of the College.

### West Pakistan

Dr. Bogen was met in Karachi by Dr. Roeinton B. Khambatta, Governor of the College, who arranged for him to visit sanatoria in the area and to meet heads of the West Pakistan Government Tuberculosis Departments.

### Philippines

Dr. Harold G. Trimble was guest of honor at a special meeting of the Philippine Chapter of the College, held at the Quezon Institute, Quezon City, on January 3, 1957. Dr. Miguel Canizares, Regent of the College for the Philippines, presided. Dr. Laureano D. Bautista, President of the Chapter, gave the opening address, followed by Dr. Manuel Quisumbing, College Governor, who introduced Dr. Trimble. Dr. Trimble, as guest Regent, inducted the officers of the Chapter for 1957.

After the induction of officers, Dr. Trimble spoke on "A Dynamic Approach to Tuberculosis" before an audience of approximately 300. He also lectured before the staff of the Ministry of Health of the Philippines at a special meeting arranged by Dr. Horace DeLien, Fellow of the College and Chief of the Health Division of the United States Operations Mission to the Philippines.

During Dr. Trimble's visit in Manila, he and Dr. Canizares called on the late President of the Republic of the Philippines, Ramon Magsaysay.

Left to right: Dr. and Mrs. Harold G. Trimble, Dr. Miguel Canizares, and the late Ramon Magsaysay, President of the Republic of the Philippines.

### East India Chapter

Dr. Trimble and Dr. Bogen presented lectures at a luncheon meeting of the East India Chapter, held in Calcutta on January 16, 1957. They were entertained by Dr. P. K. Ghosh, Governor of the College for East India, and were introduced to members of the College in the area.

### Thailand

In Bangkok, Dr. Trimble and Dr. Bogen presented lectures at a special meeting of College members and other physicians, sponsored by the Royal Thai Army Medical Department at the Army Pathology Building. More than 250 physicians attended this meeting, at which Major General Sanguan Rojanavongse, Medical Advisor of the Royal Thai Army, presided. Arrangements for the scientific session were made by Major General Thanom Upathambhananda, Surgeon General of the Army and Colonel Thip Pholpoke, Fellow of the College. Following the scientific program, Major General Sanguan Rojanavongse entertained Drs. Trimble and Bogen, their families, members of the College, and Government and Army officials at a reception at his home. During their stay in Bangkok, Drs. Trimble and Bogen visited various medical institutions in the city and were entertained at a luncheon given by the Thai members of the College.

A group at the evening party in honor of Drs. H. G. Trimble and Emil Bogen at the residence of Dr. Sanguan Rojanavongse on January 19, 1957, Bangkok, Thailand. Left to right: Commodore Kramol Champunthapongse, RTN, Deputy Surgeon General of Royal Thai Navy, Dr. Sangad Plengvanij, Director of the Department of Provincial Hospitals, Ministry of Public Health, Police Colonel Sawaeng Vajanaswasdi, Surgeon General of Police Dept., Maj. Gen. Sanguan Rojanavongse, Lady Bimol Nobharatna of the Deputy Surgeon General of the Royal Thai Army, Maj. Gen. Vibulcheep Boonlong, Deputy Under Secretary of State for the Ministry of Public Health, Prof. Kamdhorn Suvanakij, Dean of the School of Public Health, Maj. Gen. Thanom Upathambhananda, Surgeon General of the Royal Thai Army. Back row: Dr. Thip Pholpoke. Front row: (left to right) Dr. Sira Sirisambhandh, Air Vice Marshal Chua Punsori, Surgeon General of the Royal Thai Air Force and President of the Medical Association of Thailand, Dr. Emil Bogen, Dr. Sriprapai Pongaksara of the BCG Laboratory, Dr. H. G. Trimble, Dr. Banyat Prijyanond, Dr. Vaitya Chinachote, Director of T. B. Hospital. Middle row: (left to right) Dr. Thip Pholpoke, Maj. Gen. Sanguan Rojanavongse, Medical adviser to the Royal Thai Army, Dr. Sunthorn Tandhanand, Dr. Porn Piskanok. Back row: (left to right) Dr. Nadda Sriyabhai, Director of Chest Clinic, Dr. Chom Saradatta, Dr. Somsuk Bhekasut, Dr. Kamol Sinthavanondh, Dr. Praphreut Thirakupta.

### Hong Kong and China Chapter

A meeting of the Hong Kong and China Chapter was held on January 22, 1957 at 8:00 P.M. in the Ruttonjee Sanatorium and was attended by chapter members and members of the British Medical Association, Chinese Medical Association, British Institute of Radiology, and the International College of Surgeons. Dr. Mary Aquinas, President of the chapter, presided and introduced Drs. Trimble and Bogen. Dr. Bogen spoke on "Epidemiology of Tuberculosis," followed by Dr. Trimble who spoke briefly on College activities, especially the Cologne Congress. He then presented a paper on "A Dynamic Approach to Tuberculosis." A discussion period followed.

### Japanese Chapter

The annual meeting of the Japanese Chapter was held in Tokyo on January 30, 1957, at the Kitazato Memorial Hall of the Keio University School of Medicine. More than 300 physicians attended and the following scientific program was presented:

"Our Method of Endocardiac Operation Under Direct Vision"
Shigeru Sakakibara, Tokyo, Japan
"Epidemiology of Tuberculosis"
Emil Bogen, Olive View, California
"Dynamic Approach to Tuberculosis"
Harold G. Trimble, Oakland, California

A business meeting and election of officers was held after the scientific session, followed by a dinner given in honor of Drs. Trimble and Bogen and their families. Newly elected officers are:

| | |
|---|---|
| President: | Arao Imamura, Osaka |
| Vice-President: | Junjiro Okanishi, Tokyo |
| Secretary-Treasurer: | Hiroshi Sasamoto, Tokyo |

## College Chapter News

### ILLINOIS CHAPTER

The Illinois Chapter will hold its annual meeting at the Hotel Sherman, Chicago, on May 23. The following program will be presented:

9:00 a.m. William M. Lees, Chicago, President, Illinois Chapter, presiding
"Esophageal Disease"—Panel Discussion
Moderator: William E. Adams, Chicago
Panel: Albert H. Andrews, Franklin A. Kyser, and James W. C. Carpender, Chicago
"The Place of Histoplasmosis in Chest Medicine"
Henry C. Sweany, Mount Vernon, Missouri
12:00 noon Luncheon
Business meeting and election of officers.

### MICHIGAN CHAPTER

The annual meeting of the Michigan Chapter was held April 3 in Flint. Dr. Rita Tower of Flint, presented the paper "Tuberculous Tracheobronchitis—Results of the Terramycin Solution Aerosol Inhalation Therapy," which was discussed by Drs. Herbert Sloan and Winthrop N. Davey, Ann Arbor.

The following officers were elected:

| | |
|---|---|
| President: | W. Leonard Howard, Northville |
| Vice-President: | S. M. Gelenger, Flint |
| Secretary-Treasurer: | Nathan Levitt, Detroit |

### MISSOURI CHAPTER

The following officers of the Missouri Chapter were elected in Kansas City on March 31:

| | |
|---|---|
| President: | Aaron A. Sprong, Excelsior Springs |
| Vice-President: | David M. Skilling, Jr., St. Louis |
| Secretary-Treasurer: | David Nafe Kerr, St. Louis (re-elected) |

# OBITUARIES

## GROVER C. BELLINGER
## 1884-1956

Dr. Grover C. Bellinger, former superintendent of the Oregon State Tuberculosis Hospital, Salem, passed away October 24, 1956, after an illness of two years.

During Dr. Bellinger's long, active career in the fight against tuberculosis, he held many prominent offices in national and local organizations, including: Vice-president and member of the Executive Committee, National Tuberculosis Association; President, member of the Executive Committee and Advisory Board, and long-time council member, American Trudeau Society; State Tuberculosis Adviser for Selective Service in World War II; Area Consultant in Tuberculosis for the Veterans Administration; Fellow Emeritus and a past Vice-President of the American College of Chest Physicians.

He was director of the Oregon State Tuberculosis Hospital from 1913 until his retirement in 1954.

Dr. Bellinger is survived by his wife, Hattie, a daughter, Mrs. A. T. King; a son, Grover Lee Bellinger, and seven grandchildren.

William S. Conklin, M.D.
Governor for Oregon

## MARCUS W. NEWCOMB
## 1878-1957

Dr. Marcus W. Newcomb died January 18, 1957 at the age of 75, in the Burlington County Hospital, New Jersey, after a long illness. He was the former Medical Director and Superintendent of the Newcomb Chest Hospital in New Lisbon, New Jersey. Few men have made so strong an impression in both professional and public careers.

Born in Newport, New Jersey, he was educated at Newport Schools, South Jersey Institute, Peddie Institute and Jefferson Medical College where he received his medical degree in 1903. He began practicing medicine in 1904 in East Orange, New Jersey, but returned the following year to Burlington, New Jersey, where he was a general practitioner until 1912. He then became ill and moved to Browns Mills.

He opened the first private hospital for treatment of tuberculosis to be chartered by the State Board of Health in 1912 at Browns Mills, New Jersey. He managed the Browns Mills Sanitarium for ten years and then sold it to the Deborah Consumptive Relief Society of New York, the institution changing its name to the Deborah Sanitarium.

He was elected in 1919 Superintendent of the Fairview Sanitarium in New Lisbon, the tuberculosis hospital operated by Burlington County. There were four patients in the hospital at that time. He continued as Medical Director and Superintendent for thirty-two years. In 1947, the County Board of Freeholders renamed the hospital in his honor, which now has 110 beds.

Dr. Newcomb served in the New Jersey Assembly for nine years, and was majority leader in 1935 and speaker in 1936. He was a member of the Pemberton Township Board of Education for over twenty years.

He was one of the organizers of the New Jersey Chapter of the American College of Chest Physicians in 1940, and acted as the first governor. He was a former president of the Burlington County and of the New Jersey State Medical Societies, also of the Eastern Section of the American Trudeau Society, Burlington County and New Jersey State Tuberculosis Leagues.

No story of his life would be complete without mentioning his tall, lean, smiling figure; his gentle low-toned voice whether in the middle of a scientific discussion or a political address; and his devotion to his profession and work in public life.

Irving Willner, M.D.
Regent

## CALENDAR OF EVENTS

**NATIONAL AND INTERNATIONAL MEETINGS**

**23rd Annual Meeting, American College of Chest Physicians**
**Hotel Commodore, New Nork City, May 29-June 2, 1957**

**Fifth International Congress on Diseases of the Chest**
**Council on International Affairs**
**American College of Chest Physicians**
**Tokyo, Japan, September 7-11, 1958**

**CHAPTER MEETINGS**

Florida Chapter, Hollywood, May 5
Wisconsin Chapter, Milwaukee, May 5
Minnesota Chapter, St. Paul, May 12
Ohio Chapter, Columbus, May 15
Illinois Chapter, Chicago, May 23

## MEDICAL SERVICE BUREAU

### POSITIONS WANTED

**General and thoracic surgeon,** 35, F.C.C.P., desires association with clinic or established surgeon, west coast preferred. Completing 5-year residency program in July. Six years prior experience in private practice, sanatorium work, and endoscopy. Qualified for board certification in general and thoracic surgery. Please address inquiries to Box 288B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

**Chest physician,** married, 20 years hospital experience, seeks position as medical director. Available in May. References. Please address inquiries to Box 289B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

**Board certified internist,** age 37, F.C.C.P., several years' experience in private practice, would like to associate with a group or clinic. Would also be interested in a research or teaching appointment. Please send inquiries to Box 291B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

### POSITIONS AVAILABLE

**Wanted—physician** to join staff of 492-bed pulmonary disease service in large general hospital. All types of chest diseases treated. Cardiopulmonary physiology laboratory and all modern facilities available. Research encouraged. Approved for residency training. Applicants must be American citizens. Salary dependent on training and experience. Write to Director, Professional Services, VA Hospital, Memphis 15, Tennessee.

**Staff physician** wanted for California. Approved accredited bicounty hospital, pulmonary diseases (219 beds), rehabilitation chronic illness (30 beds). Starting salary $600 monthly, including furnished modern home for family. Must be eligible for California licensure. Write: Medical Director, Tulare-Kings Counties Hospital, Springville, California.

**Physician** wanted for 324-bed tuberculosis hospital, 8 miles south of Cleveland, treating all phases of chest diseases and many interesting general medical diseases. Experience not necessary. Salary up to $13,760, depending upon experience and qualifications. U. S. citizen, preferably under 54. Apply to Manager, VA Hospital, Brecksville, Ohio.

**Assistant Medical Director** wanted for 114 bed tuberculosis hospital. Salary $8500-$9500, complete maintenance. Apply Medical Director and Superintendent, District Four Tuberculosis Hospital, Ashland, Kentucky, or State Tuberculosis Hospital Commission, New State Office Building, Frankfort, Kentucky.

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